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Epilepsy in Adulthood: Prevalence, Incidence, and Associated Antiepileptic Drug Use in Autistic Adults in a State Medicaid System

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Abstract

Although epilepsy commonly presents with autism in children, it is currently unknown whether established estimates represent the prevalence and incidence of epilepsy in autistic adults. Our objective was to use population-level Medicaid data to determine prevalence, incidence, and antiepileptic drug use associated with epilepsy in a unique population of autistic adults aged 21+ with (N=2,738) and without (N=4,775) intellectual disability and to compare results to adults with intellectual disability alone (N=18,429). We found that 34.6% of autistic adults with intellectual disability and 11.1% of autistic adults without intellectual disability had epilepsy, compared to 27.0% of adults with intellectual disability alone. New incidence of epilepsy was 23.6 incident cases per 1000 person years (95% CI: 21.3, 26.2) in autistic adults with intellectual disability, 7.7 incident cases per 1000 person years (95% CI: 6.6, 8.9) in autistic adults without intellectual disability, and 15.9 incident cases per 1000 person years (95% CI: 15.2, 16.7) in adults with intellectual disability alone. Female sex and intellectual disability were associated with increased risk of prevalent and incident epilepsy in autistic adults. Findings underscore the importance of treating prevalent epilepsy and screening and preventing incident epilepsy in autistic adults as they age.

Lay Abstract

Epilepsy is more common in autistic children compared to children without autism, but we do not have good estimates of how many autistic adults have epilepsy. We used data from a full population of 7,513 autistic adults who received Medicaid in Wisconsin to figure out the proportion of autistic adults who have epilepsy, as compared to 18,429 adults with intellectual disability. We also wanted to assess how often epilepsy is first diagnosed in adulthood. Finally, we wanted to see whether antiepileptic drugs are being used to treat epilepsy in autistic adults. We found that 34.6% of autistic adults with intellectual disability and 11.1% of autistic adults without intellectual disability had epilepsy, compared to 27.0% of adults with intellectual disability alone. Autistic women and autistic adults with intellectual disability were more likely than autistic men and autistic adults without intellectual disability to have both previous and new diagnoses of epilepsy. Finally, we found that antiepileptic medications are commonly prescribed to autistic people who do not have epilepsy potentially to treat mental health conditions or behavior problems, and that antiepileptic medications are not always prescribed to autistic people with

epilepsy even though they are indicated as a first-line epilepsy treatment. The findings of this study highlight the need to effectively treat and prevent epilepsy in autistic adults.

Keywords

Autism Spectrum Disorders; Epilepsy; Medicaid; Intellectual Disability; Gender; Sex Differences; Stroke; Medical Comorbidity

Introduction

Epilepsy affects approximately 1–2% of children and adults in the United States (Zack & Kobau, 2017), and epilepsy's co-occurrence with autism spectrum disorder (ASD) has been well-documented since autism was first described by Kanner (1943). Current prevalence estimates for epilepsy in autistic people vary: studies find that 1.8 to 60% of autistic people having epilepsy, with a meta-analytic prevalence estimate at 12.1% (Lukmanji et al., 2019). The high co-occurrence of epilepsy and ASD is a rich area for subgroup research, as the presence of both conditions may signal a different biological etiology or genetic condition (Amiet et al., 2008). Further, there is momentum in the advocate and research community to better understand how epilepsy both presents in autistic adults and impacts and impairs their daily life so that adult-specific services and treatments can be developed and targeted.

Epilepsy is associated with reduced quality of life (McGrother et al., 2006; Ramsey, Loiselle, Rausch, Harrison, & Modi, 2016) and is a strong predictor of premature mortality (Hirvikoski et al., 2016; Pickett, Xiu, Tuchman, Dawson, & Lajonchere, 2011; Rubenstein & Bishop-Fitzpatrick, 2018) for autistic adults. Higher risk of death in autistic people with epilepsy is due to a combination of epilepsy complications including sudden unexplained death in epilepsy (SUDEP), status epilepticus (i.e., a seizure lasting more than 30 minutes *or* two seizures or more without full recovery of consciousness in between seizures), and seizure-related accidents (e.g., trauma, drowning, accidental injury). In their longitudinal community-based study, Gillberg, Billstedt, Sundh, and Gillberg (2010) found that epilepsy and cognitive impairment were associated with increased mortality risk in autistic adults. Through use of the 2006 California Department of Developmental Services Mortality Data, Pickett et al. (2011) calculated the death rate for those with ASD alone, epilepsy alone, and ASD with epilepsy. Their findings indicated that autistic people with epilepsy were at higher risk of death compared to people with ASD or epilepsy alone. Finally, Hirvikoski et al. (2016) reported that the most common cause of death in autistic adults with intellectual disability (ID) is epilepsy, which is likely associated with the high prevalence of epilepsy in autistic adults with ID and the high mortality burden related to SUDEP, status epilepticus, and seizure-related accidents in people with epilepsy.

The clinical overlap between epilepsy and ASD is well-established: epilepsy is more prevalent in autistic children than in children who are not autistic, and ASD is more prevalent in children with epilepsy than in children without epilepsy (Besag, 2018). These patterns are consistent and clear in children but may be different in autistic adults. Epilepsy can develop later in life, as incidence of epilepsy is greater in adults aged 65 and older compared to young adults in the general population, with common causes of incident

epilepsy in adults aged 65 and older being cerebrovascular disease (including stroke), neurodegenerative disorders, traumatic brain injuries, and intracerebral tumors (Brodie, Elder, & Kwan, 2009). Whether the condition started in childhood or in adulthood has a large influence on child development or adult loss of adaptive and cognitive functioning (Smith, 2010). Since the majority of the population of autistic people are young (Rubenstein & Bishop, 2019) we know relatively little about whether there is a incidence of new epilepsy in autistic adults. The lack of knowledge about incident epilepsy in adulthood substantially limits our ability to address co-occurring epilepsy in the context of ASD.

In a recent meta-analysis, epilepsy was found to be more prevalent in autistic females (19%) compared to autistic males (11%; Lukmanji et al., 2019). An older meta-analysis found that the pooled prevalence of epilepsy was higher in autistic people with ID (21.5%) compared to autistic people without ID (8.0%; Amiet et al., 2008). The question remains as to whether these epidemiological estimates stratified by sex and ID hold as autistic people age or whether autistic people develop incident epilepsy in adulthood. In our preliminary data, we found that the odds of epilepsy in Medicaid claims for middle aged and older autistic adults (aged 40+) with co-occurring ID were 2.2 times that of middle aged and older autistic adults without ID (Bishop-Fitzpatrick & Rubenstein, 2019). However, these data were limited to older autistic adults with only three years of follow up, and a more focused assessment over a longer time period with an ID control group is needed.

Although the best performing algorithms for identifying epilepsy in claims data combine diagnostic (diagnostic codes) and antiepileptic prescription data (Moura, Price, Cole, Hoch, & Hsu, 2017), there are problems with relying on prescription drug data when examining the prevalence and incidence of epilepsy in autistic people. One potential complication in assessing epilepsy in this population is that antiepileptic drugs are often used off-label to treat mental health conditions and behavior problems (for review, see: Di Martino & Tuchman, 2001), leading to the potential for misclassification if classification of epilepsy is based on antiepileptic drug prescriptions alone. Differences in use of antiepileptic drugs in autistic people also have important implications for health service utilization in that lack of concordance between diagnostic codes for epilepsy and prescriptions for antiepileptic drugs may signal a disparity in the receipt of evidence-based epilepsy care or the presence of burdensome side effects of antiepileptic medications. It is crucial to better understand how these epileptic drugs are prescribed in the adult autistic population, and how that corresponds to claims for epilepsy.

Using health systems data, including Medicaid claims, is one of the most rigorous ways we currently have of assessing population-level health in autistic adults (Rubenstein & Bishop, 2019). While using Medicaid claims data is limited to adults with identified autism (and misses autistic adults who have not been formally diagnosed), it does allow us to make inferences about the population that receives publicly funded services for ASD. Our goal was to leverage 11 years of medical claims data on all autistic adults identified and served in the Wisconsin Medicaid system to better understand the prevalence and incidence of epilepsy in autistic adults. We compared prevalence of epilepsy in autistic adults to adults with ID without ASD as a control group, using both a 2-year and 11-year period prevalence to examine whether epilepsy prevalence differs depending on the time frame. We

hypothesized that we would find similar prevalence rates of epilepsy in our adult sample compared to samples of autistic children, and that two-year and 11-year period prevalence would be similar. We also compared incidence of epilepsy in autistic adults to adults with ID and without ASD. We hypothesized that we would find evidence of incident epilepsy in adulthood. We then examined whether sex and ID status increased prevalence of epilepsy as seen in other samples, and we assessed whether there was an interactive effect of sex and ID in increasing probability of having epilepsy. We hypothesized that prevalence and incidence of epilepsy would be higher in autistic adults with ID compared to autistic adults without ID and that it would be more prevalent in women compared to men. Lastly, we examined antiepileptic drug prescriptions to explore whether having a claim for epilepsy is concordant with having a prescription for antiepileptic drugs in the Medicaid data. We hypothesized that we would identify adults with claims for antiepileptic drugs without medical claims for epilepsy.

Methods

Data source

We obtained data from the Wisconsin Department of Health Services Medicaid program for the years January 1, 2008 to December 31, 2018. In Wisconsin, Medicaid is an anti-poverty program that provides health care coverage to low income and disabled people; therefore, Medicaid data is a useful tool to assess health in autistic people at the population level, especially with the increase in young autistic people served by Medicaid (Rubenstein & Bishop, 2019). The Department of Health Services identified enrollees with a past claim for ASD or ID at any point in their enrollment history, then provided demographic information (age, race/ethnicity, sex, county of residence); medical claims (dental claims, home health claims, long-term care claims, pharmacy claims and professional, inpatient, and outpatient claims and crossover claims; hospital-based acute care claims not included) and their corresponding International Classification of Disease (ICD)-9 or ICD-10 and their month and year; and paid amount for each claim. Our sample included 4,775 unique beneficiaries with ASD without ID (ASD without ID group); 2,738 ASD with ID (ASD+ID group); and 18,429 with ID without ASD (ID group). Further detail is available in Rubenstein and Bishop (2019).

Epilepsy/Seizure

We identified the presence of epilepsy using the Chronic Conditions Data Warehouse (CCW) Condition Category for epilepsy using ICD-9 and ICD-10 codes (See Supplement 1). To ensure accuracy in diagnosis, we considered two claims to indicate presence of an epilepsy/seizure condition. Additionally, we identified the first epilepsy claim in our data for each beneficiary so we could further assess incidence.

Epilepsy Medications

We created a list of medications prescribed for epilepsy (see Supplement) from published guidelines (Goldenberg, 2010; Vossler, Weingarten, Gidal, & American Epilepsy Society Treatments Committee, 2018) then examined all pharmacy claims for identified prescriptions. We were unable to match pharmacy claims to other medical claims because

we did not have data on the day of the claim, and prescriptions are not always filled on the day they are prescribed.

Analysis

We presented descriptive statistics for demographic characteristics and enrollment, as well as prevalence of health conditions known to be associated with increased risk of epilepsy in older adulthood (aged 65 and older) in the general population (Brodie et al., 2009). We used log binomial regression to calculate 11-year period prevalence (2008–2018) and two-year prevalence (2017–2018). Epilepsy was considered prevalent if a beneficiary had two claims for epilepsy at any time in the period. To assess for difference in epilepsy across the lifespan (Brodie et al., 2009) we included age at first claim in our data into the model (<30, 30–39, 40–49, 50–59, 60+) and tested whether any of the categories significantly differed from one another using a Type-III F test. We assessed prevalence over the entire 11-year period and in just the last two years of data to capture a longer-period prevalence (11 years) and a shorter point prevalence (2-years). Assessing prevalence over two timespans allows us to examine temporal trends and our ability to capture epilepsy prevalence in a shorter time frame. To calculate incidence, we used log-Poisson regression to model incidence by age category using a two-year wash-out period (i.e., a person had to be enrolled for one or two years in our data without receiving an epilepsy claim to be included in the denominator).

To assess association between epilepsy, sex, and ID, we ran log-binomial regression to calculate prevalence ratios and log-Poisson regression to calculate incidence rate ratios. In both models, we included a term for sex, ID, and an interaction term between the two. We also included terms for categorical age at first year in which we had data for an individual beneficiary, and number of years enrolled to account for different cohort patterns (Rubenstein & Bishop, 2019).

Additionally, we assessed concordance between epilepsy diagnostic claims and antiepileptic medication prescription claims. We used a Cochrane Mantel-Hanzel test to examine whether the relationship between epilepsy claims and antiepileptic drug prescription claims differed by group.

Results

Demographics

Demographic characteristics are displayed in Table 1. A higher proportion of beneficiaries in the ASD+ID (68%) and ASD without ID (73%) groups were male compared to the ID group (51%). The majority of the sample in each group was white, although there were considerable missing race data. More than half the ASD without ID group was less than 30 years old in their first year of claims. Further description of enrollment age and enrollment trends can be found in Rubenstein and Bishop (2019). By epilepsy status, mean and median age were similar but a higher percentage of those without epilepsy were <30 years old. Prevalence of stroke, dementia, traumatic brain injury, and headaches was higher in those with epilepsy compared to those without for all groups (post-hoc chi square tests; $p<0.05$).

Prevalence

Estimated prevalence and incidence of epilepsy in our sample are presented in Table 2 and Table 3. Overall in the ASD without ID group, the 11-year period prevalence was 11.1 cases of epilepsy per 100 enrollees (95% confidence interval: 10.2, 12.5). In contrast, prevalence in the ASD+ID group over the 11-year period was 34.6 per 100 (95% CI: 32.8, 36.4) and prevalence in the ID group was 27.0 per 100 (95% CI: 26.3, 27.6). For two-year prevalence, prevalence estimates were similar to the 11-year period: the ASD without ID group (N=2,738 enrolled in the two year period) prevalence was 11.5 per 100 (95% CI: 10.6, 12.5), ASD+ID (N=2,497 enrolled in the two year period) was 33.6 (95% CI: 31.8, 35.5) and in the ID only group (N=14,546 enrolled in the two year period) prevalence was 26.4 per 100 (25.6, 27.1). For all models, categorical age indicators significantly differed from one another as a group at an alpha=0.05 level, so we present age specific prevalence as well which illustrates cohort and age effects.

Incidence

When assessing incidence using a 2-year washout (Table 3), 176 adults in the ASD without ID group had an incidence claim for epilepsy for a rate of 7.7 incident cases of epilepsy per 1000 person years (95% CI: 6.6, 8.9), 365 adults with ASD with ID had an incident claim of epilepsy for a rate 23.6 cases per 1000 person years (95% CI: 21.3, 26.2), and 1747 adults with ID had an incident claim of epilepsy for a rate of 15.9 cases of epilepsy per 1000 person years (95% CI: 15.2, 16.7). While incidence increased after age 50 in the ASD+ID and ID only groups, autistic adults without ID aged 40–49 had the highest incidence of epilepsy. Of note, 10 strokes preceded epilepsy in autistic adults without ID, 8 strokes preceded epilepsy in autistic adults with ID, and 140 strokes preceded epilepsy in adults with ID.

Effect of Sex and ID

In both the 11-year and 2-year prevalence periods, female sex was significantly associated with epilepsy in autistic adults (with and without ID; Prevalence Ratio (RR): 1.21, 1.20 respectively; Table 4). For autistic adults with ID, prevalence of epilepsy was 2.65 (95% CI: 2.3, 3.0) times that of autistic adults without ID in the 2008–2018 period and 2.37 (95% CI: 2.1, 2.7) times that of autistic adults without ID in the 2017–2018 period. The interaction effect between sex and ID status was not statically significant in either period (2008–2018 period: $p = 0.4$; 2017–2018 period: $p = 0.1$).

Results were similar when assessing incident rate ratio. Incidence of epilepsy in female autistic adults was 1.26 (95% CI: 1.0, 1.7) times that of male autistic adults in 2008 to 2018 and 1.11 (95% CI: 0.8, 1.5) in 2017–2018. ID was significantly associated with increased incidence of epilepsy, and again, there was no significant interaction effect (2008–2018 period: $p = 0.9$; 2017–2018 period: $p = 0.2$).

Medication

Results of our analysis of the concordance between epilepsy and medication claims are reported in Table 5. Comparing epilepsy diagnostic claims to antiepileptic prescription claims, we found that 80.3% of enrollees with ASD without ID who had received anti-

epileptic medications did not have a claim for epilepsy: the percentage was 55.9% in the ASD with ID group and 60.2% in the ID group. For those with epilepsy diagnostic claims, 71.4% in the ASD without ID group, 79.6% in the ASD with ID group, and 62.3% in the ID group had a prescription claim for antiepileptic medication. The case groups significantly differed in their associations between medication use and diagnostic claims (CMH $p<0.0001$).

Discussion

Although high prevalence of epilepsy has been replicated in population-based samples of autistic children, these current estimates may not represent the population-level impact of epilepsy in autistic adults. We used data from a state Medicaid system to confirm high prevalence of epilepsy and examine incident epilepsy in autistic adults. Epilepsy is associated with high burden in affected individuals and impairs daily living and quality of life (McGrother et al., 2006; Ramsey et al., 2016). Assessing factors associated with occurrence and treatment of epilepsy can help guide future prevention efforts and improve treatment delivery.

We found that over an 11-year period, 34.6% of autistic adults with ID and 11.1% in autistic adults without ID had epilepsy as identified in medical claims. The 11-year period allowed us to assess the maximum amount of people enrolled in our data and their available claims. A two-year prevalence period resulted in similar prevalence, which suggests that epilepsy in autistic people and people with intellectual disabilities can be adequately captured in a shorter period of claims data. Our prevalence figures for epilepsy are in the range of previous estimates of epilepsy prevalence in mixed groups of autistic adults with and without intellectual disability that range from 11.94% (Croen et al.. 2015) to 25.4% (McDermott et al., 2005) to 38.3% (Giovanardi Rossi, Posar, & Parmeggiani, 2000). Prevalence of epilepsy for adults with ID alone (27.0%) was greater than the ASD without ID group and less than the ASD with ID group. This implies that ID alone does not entirely explain the occurrence of epilepsy in autistic people, especially since the population prevalence of epilepsy in adults is 1.2% (Zack & Kobau, 2017). This pattern of epilepsy prevalence (ASD+ID>ID>ASD only) was also similar when assessing epilepsy incidence. The incidence of epilepsy in adulthood may be due to other health conditions such as stroke, dementia, or traumatic brain injury (Brodie et al., 2009) and we did see differences in prevalence of stroke, dementia, and traumatic brain injury between those with epilepsy and those without within each case group. It will be important to continue to monitor incident epilepsy as autistic adults age into older adulthood. With a larger sample of older adults and more detailed medical data, research can identify causal mechanisms of epilepsy incidence in autistic adults and develop preventative approaches.

Association between Epilepsy and Age

In our sample, epilepsy prevalence was impacted by age, yet there were no clear age-related trends across age categories in autistic adults without ID. For autistic adults with ID and adults with ID alone there was increasing prevalence with increasing age (until the oldest category in which death likely attenuated estimates; Hirvikoski et al., 2016; Pickett et al.,

2011; Rubenstein & Bishop-Fitzpatrick, 2018), as would be expected with the chronicity of prevalent epilepsy plus the incidence of new cases. The lack of an association between age and epilepsy prevalence in autistic adults without ID could be due to cohort effects, as older autistic adults without ID are likely very different from younger autistic adults without ID (Rubenstein & Bishop, 2019). Patterns in incident epilepsy were less clear. As the autistic population continues to age, these age-trends may differ and may have larger public health implications as larger cohorts may be at risk of incident epilepsy.

Association between Epilepsy and Intellectual Disability

As seen in these epidemiological data, prevalence and incidence of epilepsy is especially high in people with ID with and without co-occurring ASD. ASD, ID, and epilepsy may all occur together because of specific genetic conditions. Single gene disorders, such as tuberous sclerosis and fragile X syndrome, are associated with all three conditions and may share causal mechanisms in alterations to transcriptional regulation, cellular growth, synaptic structure, and synaptic channels (Besag, 2018; Lee, Smith, & Paciorkowski, 2015). Further, autistic adults with ID may be at increased risk for other health conditions associated with incident epilepsy in older adulthood. We found that headaches and migraines, risk factors for late onset epilepsy, were more prevalent in older autistic adults with ID compared to older autistic adults without ID (Bishop-Fitzpatrick & Rubenstein, 2019). There is also some evidence that dementia is more prevalent in autistic adults with ID compared to autistic adults without ID, with dementia being another risk factor for incident epilepsy in older adulthood (Bishop-Fitzpatrick & Rubenstein, 2019; Brodie et al., 2009; Croen et al., 2015). Signs of epilepsy should be closely watched for in older autistic adults with ID and more work needs to be done to understand mechanisms underlying incident epilepsy for this population.

Epilepsy in Autistic Women

In our sample, prevalence of epilepsy in autistic women was 1.2 times that of autistic men. This finding aligns with the theory that difference in epilepsy prevalence between the sexes is partially attributable to ASD identification: in order to get an ASD diagnosis females have to present with a more severe presentation (Dworzynski, Ronald, Bolton, & Happé, 2012) and a more severe presentation is associated with increased risk of epilepsy (Kirkovski, Enticott, & Fitzgerald, 2013). Autistic females may have a higher genetic/etiologic burden (Robinson, Lichtenstein, Anckarsäter, Happé, & Ronald, 2013) and a greater mutational load which may also increase epilepsy risk (Blackmon et al., 2016). Notably, we did not identify a significant interaction effect between sex and ID. Being female with ID did not confer any additional risk of epilepsy than the individual effects of being female and having ID, which may be an etiologic clue to sex-specific epilepsy development to examine in future work.

Concordance between Epilepsy Claims and Antiepileptic Medication Use

When examining concordance between epilepsy claims and antiepileptic drug prescriptions, we found that more than 25% of autistic adults without ID and 20% of autistic adults with ID had claims for epilepsy and did not receive epilepsy medication. Antiepileptic drugs are often indicated as front-line treatments for epilepsy and lack of claims for antiepileptic drugs in autistic adults with claims for epilepsy may be indicative of disparities in receipt of

evidence-based epilepsy care. Alternatively, antiepileptic medication often causes burdensome side effects (Chen et al., 2017) and it is possible that psychiatric and behavioral side effects are particularly burdensome for autistic people and their caretakers. Autistic people may elect to not take the medication in order to avoid the medication's side effects. In all groups, antiepileptic medication was most often prescribed to individuals without claims for epilepsy. Antiepileptic drugs (e.g., valproate and carbamazepine) are commonly prescribed off label for mental health conditions and challenging behaviors (Di Martino & Tuchman, 2001), which makes researching epilepsy treatments and services challenging in claims data. For many conditions in claims data, a prescription claim can be an indicator of the presence of a certain health condition in an individual. We illustrate that this is not the case for ASD and epilepsy. Additional phenotypic data will help us better understand predictors of off-label use and better differentiate those with epilepsy and those on antiepileptic medications.

Limitations

Although Medicaid data allows us to assess population-level medical claims data across an entire state health care system, these data have inherent limitations. Like all claims data, these data may be more accurate at capturing chronic medical conditions such as epilepsy and stroke and less accurate at capturing less serious medical problems such as headaches. Second, diagnoses for ASD, ID, and epilepsy were not validated by a standardized clinical examination outside of examinations performed by clinicians when entering claims. Similarly, because diagnoses for ASD and ID were not clinically validated, it is possible that there were some diagnostic inaccuracies. Although previous research finds that claims-based identification of ASD in children tracks well with criterion standard assessment (Dodds et al., 2009) and diagnosis based on review of medical records (Fombonne et al., 2004), the validity of identification of ASD in adults in Medicaid claims data has not been specifically tested. Finally, although this sample is likely more diverse than clinically ascertained samples, because of missing data on race, this study could not closely evaluate differences by race. Thus, findings may be limitedly generalizable to autistic people from marginalized racial and/or ethnic groups.

We are only able to assess those that meet Wisconsin Medicaid eligibility criteria and who had claims for ASD or ID; therefore, some individuals who might qualify for an ASD or ID diagnosis after clinical assessment were not captured by our data due to income and/or assets above Medicaid eligibility limits or lack of opportunity to get a formal diagnosis. Under-ascertainment may be particularly high among older autistic adults who are subject to cohort effects in access to diagnosis for and treatment of ASD (Rubenstein & Bishop, 2019).

Conclusions

Epilepsy is a condition that co-occurs with ASD that increases risk of mortality and lowers quality of life. Our findings on prevalence and incidence of epilepsy in autistic adults highlight the importance of treating prevalent epilepsy and preventing and screening incident epilepsy as autistic adults age, particularly in autistic women and in autistic adults with ID. Intellectual disability and sex may be pivotal areas to target treatment and identify subgroup specific etiology in future research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographics of autistic adults and adults with intellectual disability in Wisconsin Medicaid 2007–2018, by epilepsy status

	Autism without Intellectual Disability (N=4775)		Autism with Intellectual Disability (N=2738)		Intellectual Disability (N=18429)	
	With epilepsy N (%) N=529	Without epilepsy N (%) N=4246	With epilepsy N (%) N=946	Without epilepsy N (%) N=1792	With epilepsy N (%) N=4969	Without epilepsy N (%) N=13460
Sex						
Male	357 (67.5)	3143 (74.0)	647 (68.4)	1228 (68.5)	2563 (51.6)	6894 (51.2)
Female	172 (32.5)	1103 (26.0)	299 (31.6)	564 (31.5)	2406 (48.4)	6566 (48.8)
Race/Ethnicity						
White	301 (56.9)	2557 (60.2)	570 (60.3)	1097 (61.2)	3216 (64.7)	8411 (62.5)
Black	27 (5.1)	222 (5.2)	74 (7.8)	154 (8.6)	389 (7.8)	1097 (8.2)
Other	6 (1.1)	70 (1.6)	9 (1.0)	29 (1.6)	92 (1.9)	285 (2.1)
Hispanic	9 (1.7)	99 (2.3)	15 (1.6)	41 (2.3)	121 (2.4)	302 (2.2)
Missing	186 (35.1)	1298 (30.6)	278 (29.4)	471 (26.2)	1171 (23.6)	3365 (25.0)
County type						
Rural	85 (16.0)	864 (20.3)	177 (18.7)	328 (18.3)	1083 (21.8)	3090 (23.0)
Urban	444 (84.0)	3382 (79.7)	769 (81.3)	1464 (81.7)	3886 (78.2)	10370 (77.0)
Age[a]						
<30	263 (49.7)	2437 (57.4)	194 (20.5)	511 (28.5)	523 (10.5)	1921 (14.3)
30–39	150 (28.4)	1030 (24.3)	252 (26.6)	453 (25.3)	880 (17.7)	2445 (18.2)
40–49	65 (12.3)	399 (9.4)	163 (17.2)	281 (15.7)	876 (17.6)	2192 (16.3)
50–59	28 (5.3)	209 (4.9)	200 (21.1)	300 (16.7)	1228 (24.7)	2934 (21.8)
≥60	23 (4.3)	171 (4.0)	137 (14.5)	247 (13.8))	1462 (29.4)	3969 (29.5)
Mean (SD)	26.7 (10.0)	26.7 (2.5)	33.7 (13.6)	33.2 (13.7)	41.9 (16.2)	41.9 (16.6)
Median (IQR)	22 (7)	22 (7)	29 (22)	28 (22)	42 (26)	41 (28)
Years Enrolled						
Enrolled 2017–2018	490 (92.6)	3778 (89.0)	838 (88.6)	1659 (92.6)	3833 (77.1)	10713 (79.6)
Mean (SD)	7.5 (3.2)	6.0 (3.3)	9.5 (2.4)	8.8 (3.0)	9.1 (2.7)	8.4 (3.1)
Median (IQR)	8 (6)	5 (6)	11 (3)	11 (4)	11 (4)	10 (5)
Central Nervous System Risk Factors						
Stroke	17 (3.2)	28 (0.7)	39 (4.0)	39 (2.2)	430 (8.7)	476 (3.5)
Dementia	29 (5.5)	104 (2.4)	122 (12.9)	148 (8.3)	971 (19.5)	1866 (13.9)
Traumatic brain injury	4 (0.8)	9 (0.2)	11 (1.2)	9 (0.5)	165 (3.3)	108 (0.8)
Headache	62(11.7)	428 (10.1)	57 (2.1)	113 (4.1)	575 (11.6)	1242 (9.2)

[a] Age represents age at time of entry into the data.

Table 2

Prevalence of epilepsy per 100 (95% CI) autistic adults and adults with intellectual disability in Wisconsin Medicaid

	Autism without Intellectual Disability		Autism with Intellectual Disability		Intellectual Disability	
	2008–2018	2017–2018	2008–2018	2017–2018	2008–2018	2017–2018
	N=4775	N=4268	N=2738	N=2497	N=18429	N=14546
Overall	11.1 (10.2, 12.0)	11.5 (10.6, 12.5)	34.6 (32.8, 36.4)	33.6 (31.8, 35.5)	27.0 (26.3, 27.6)	26.4 (25.6, 27.1)
Age <30	9.7 (8.6, 10.9)	10.0 (8.8, 11.2)	27.5 (24.4, 31.0)	27.9 (24.7, 31.5)	21.4 (19.8, 23.1)	20.9 (19.3, 22.7)
Age 30–39	12.7 (11.0, 14.8)	13.3 (11.4, 15.4)	35.7 (32.4, 39.5)	35.3 (31.9, 39.1)	26.5 (25.0, 28.0)	25.9 (24.3, 27.5)
Age 40–49	14.0 (11.2, 17.6)	15.1 (12.0, 19.1)	36.7 (32.5, 41.5)	35.5 (31.1, 40.1)	28.6 (27.0, 30.2)	27.5 (25.8, 29.3)
Age 50–59	11.8 (8.3, 16.7)	12.4 (8.6, 18.0)	40.0 (35.9, 44.5)	38.1 (33.8, 43.0)	29.5 (28.2, 30.1)	27.7 (26.3, 29.3)
Age ≥60	11.9 (8.0, 17.4)	12.2 (8.0, 18.6)	27.5 (24.4, 31.0)	33.1 (28.4, 38.7)	26.9 (25.8, 28.1)	27.8 (26.4, 29.3)

Table 3

Incidence of epilepsy per 1000 person years (95% CI) in autistic adults and adults with intellectual disability in Wisconsin Medicaid

	Autism without Intellectual Disability	Autism with Intellectual Disability	Intellectual Disability
	N=3655	N=2054	N=14252
Overall	7.7 (6.6, 8.9)	23.6 (21.3, 26.2)	15.9 (15.2, 16.7)
Age <30	6.8 (5.3, 8.9)	22.9 (17.6, 29.7)	14.0 (11.7, 16.7)
Age 30–39	6.6 (5.1, 8.6)	20.3 (16.5, 24.9)	11.5 (10.2, 13.0)
Age 40–49	11.4 (8.2, 15.9)	19.8 (15.3, 25.8)	15.7 (14.0, 17.5)
Age 50–59	8.6 (5.1, 14.8)	28.7 (23.3, 35.3)	18.0 (16.5, 19.7)
Age ≥60	10.4 (6.1, 17.5)	28.1 (22.4, 35.4)	17.8 (16.4, 19.3)

Table 4

Differences by Sex and ID in Prevalent and Incident Epilepsy in Adults with Autism enrolled in 2007–2018

	2008–2018		2017–2018	
	Prevalence Ratio	**95% CI**	**Prevalence Ratio**	**95% CI**
Female vs Male	1.21	1.0, 1.5	1.20	1.0, 1.4
ID vs No ID	2.65	2.3, 3.0	2.37	2.1, 2.7
Female × ID interaction	0.81	0.7, 1.0	0.84	0.7, 1.0
	2008–2018		**2017–2018**	
	Incidence Rate Ratio	**95% CI**	**Incidence Rate Ratio**	**95% CI**
Female vs Male	1.26	1.0, 1.7	1.11	0.8, 1.5
ID vs No ID	2.83	2.3, 3.5	2.52	2.0, 3.2
Female × ID interaction	0.81	0.6, 1.1	1.02	0.7, 1.5

Model included age category, years enrolled, sex, ID status, and sex by ID interaction term

ID: Intellectual disability

Table 5

Concordance between epilepsy medical claims and antiepileptic drug prescription claims in autistic adults and adults with ID in Wisconsin Medicaid 2007–2018

	Autism without Intellectual Disability (N=4775)			Autism with Intellectual Disability (N=2738)			Intellectual Disability (N=18429)		
Epilepsy claim	**Antiepileptic Medication**			**Antiepileptic Medication**			**Antiepileptic Medication**		
	Yes	**No**	**Row Total**	**Yes**	**No**	**Row Total**	**Yes**	**No**	**Row Total**
Yes	378	151	529	753	193	946	3097	1872	4969
No	1539	2707	4246	955	837	1792	4686	8774	13460
Column Total	1917	2858		1708	1030		7783	10646	