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Diagnosis and pharmacological management of attention deficit hyperactivity disorder in adults with and without intellectual disability: cohort study using electronic health records

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Abstract

Background. Attention deficit hyperactivity disorder (ADHD) is increasingly diagnosed in adults. People with intellectual disability have higher rates of ADHD yet there is little evidence on the presentation and pharmacological treatment of ADHD in this population or how this differs from the general population.

Methods. Retrospective cohort study using data from electronic health records. Adults with intellectual disability newly diagnosed with ADHD between 2007 and 2022 were matched to adults with ADHD without intellectual disability and their clinical features and treatments were compared.

Results. A total of 159 adults with ADHD and intellectual disability and 648 adults with ADHD without intellectual disability formed the dataset. Adults with intellectual disability had higher rates of psychiatric co-morbidity and spent more time under mental health services than those without intellectual disability. They were more likely to have recorded agitation, aggression, hostility, and mood instability, and less likely to have poor concentration recorded in the 12 months prior to the diagnosis of ADHD. Following diagnosis, people with intellectual disability were significantly less likely to be prescribed any medication for ADHD than controls without intellectual disability (adjusted odds ratio 0.60, 95% confidence interval 0.38–0.91), and were less likely to be prescribed stimulants (27.7% *v* 46.0%, $p < 0.001$).

Conclusions. The presence of behaviors that challenge in adults with intellectual disability may indicate co-occurring ADHD. Further work to define the safety and efficacy of medication for ADHD in adults with intellectual disability is needed to understand differences in prescription rates and to avoid inequities in care outcomes.

Introduction

Intellectual disability, also known as learning disability, is a lifelong neurodevelopmental disorder defined by significantly below average intellectual functioning and impaired adaptive behavior (World Health Organization, 2022). The global prevalence of intellectual disability is around 1%, with higher rates in males and those living in low and middle-income countries (Maulik, Mascarenhas, Mathers, Dua, & Saxena, 2011). Intellectual disability may be caused by genetic abnormalities, by problems before or during birth, or by disruption to brain development during childhood due to infection or traumatic injury. People with intellectual disability often have co-occurring neurodevelopmental conditions such as autism are more likely than those in the general population to experience mental illness (Mazza, Rossetti, Crespi, & Clerici, 2020; McClain, Mills, & Murphy, 2017).

Attention deficit hyperactivity disorder (ADHD) describes a pattern of inattentive and/or hyperactive-impulsive symptoms that adversely impact an individual's functioning across several domains. The symptoms occur across different settings and are present before the age of 12 years (World Health Organization, 2022). Although traditionally understood as a disorder of childhood and adolescence that largely resolves by young adulthood (Hill & Schoener, 1996; Zalsman & Shilton, 2016), longitudinal studies have now shown that clinically significant symptoms of ADHD frequently persist into adulthood, and the disorder is recognized to affect people across the lifespan (Di Lorenzo et al., 2021; Uchida, Spencer, Faraone, & Biederman, 2018). The rate of diagnosis of ADHD in adults is increasing, likely due to increasing awareness among professionals and the public, and the expansion of diagnostic criteria over the past decade (Chung et al., 2019; Fairman, Peckham, & Sclar, 2020).

The point prevalence of ADHD in adults in the general population has been estimated at around 2.5% (Faraone et al., 2021; Fayyad et al., 2017). The corresponding prevalence in adults with intellectual disability is generally accepted to be significantly higher (Thapar, 2017) but

has been difficult to accurately define owing to differences in methodological approaches, case ascertainment, and sampling frames (Reilly & Holland, 2011). Studies have estimated that ADHD may be present in up to 20% of adults with intellectual disability (La Malfa, Lassi, Bertelli, Pallanti, & Albertini, 2008) and may be even more prevalent in people with certain genetic conditions associated with intellectual disability, including Down syndrome and Fragile X syndrome (Lo-Castro, D'Agati, & Curatolo, 2011).

ADHD may be under-recognized and under-diagnosed in adults with intellectual disability. Diagnostic overshadowing can mean that symptoms of ADHD are misattributed to the intellectual disability and not considered a separate condition and a target for treatment (Simonoff, Pickles, Wood, Gringras, & Chadwick, 2007). Screening and diagnostic tools developed for use in the general population have not been validated in people with intellectual disability (Perera, Courtenay, Solomou, Borakati, & Strydom, 2020). Standard diagnostic criteria may be less relevant to people with intellectual disability and some symptoms may not be applicable (Perera, 2018; Seager & O'Brien, 2003). Co-occurring autism, verbal communication difficulties, and other mental disorders may complicate the clinical picture and impinge on the diagnosis of ADHD. Specialist clinicians with training in intellectual disability may not be available, further limiting opportunities for recognition and accurate diagnosis.

Medication is recommended as first-line management in adults with ADHD (Bolea-Alamanac et al., 2014; National Institute for Health & Care Excellence, 2018). Stimulant drugs (e.g. methylphenidate, dexamfetamine) and non-stimulant drugs (e.g. atomoxetine) are licensed for treatment and have different neurobiological effects, onset/duration of action, and side-effect profiles (Bolea-Alamanac et al., 2014). There is a paucity of evidence on the use and efficacy of ADHD medication in adults with intellectual disability.

To the best of our knowledge, there is no research comparing newly diagnosed ADHD and its clinical presentation in adults with intellectual disability to the general population with ADHD. Furthermore, the pharmacological treatment of ADHD in intellectual disability is currently understudied and patterns of prescribing are poorly understood. The aim of this study was to investigate the pre-diagnosis presentation and post-diagnosis pharmacological treatment of newly diagnosed ADHD in adulthood and compare these between people with and without intellectual disability by conducting a retrospective cohort study using routinely collected health data.

Methods

Study setting

Data were obtained from the South London and Maudsley (SLaM) National Health Service (NHS) Biomedical Research Centre (BRC) in England. SLaM is the largest provider of mental healthcare in Europe, with a catchment area that covers four socio-demographically diverse south London boroughs with a combined population of ~1.3 million people. The trust provides a wide range of community and in-patient mental health services, including specialist diagnostic clinics and services for people with intellectual disability.

ADHD should be diagnosed by a specialist clinician in secondary care (National Institute for Health and Care Excellence, 2018). Diagnoses within SLaM may be made in specialist ADHD services, in general mental health teams, or in teams providing services for people with intellectual disability. A new diagnosis of ADHD is recommended to be made based on a thorough assessment which typically includes a full clinical and psychosocial evaluation, developmental history, application of standardized questionnaires, and informant reports (National Institute for Health and Care Excellence, 2018; Royal College of Psychiatrists, 2021). Following a diagnosis of ADHD, management options are discussed. Medication can only be initiated by a specialist, most likely in the clinic where the original diagnosis was made; after a period of time and when the patient is stable, they may be discharged with ongoing prescribing and monitoring undertaken by their primary care physician (South East London Integrated Medicines Optimisation Committee, 2020).

Data source

A full electronic health record (EHR) has operated in all SLaM services since 2006; each patient's record contains structured clinical information (demographic details, diagnoses, contacts with professionals) and detailed information related to their history, presenting problems, diagnostic formulation, and care plans, that is added by health professionals in the form of free text and uploaded documents (e.g. correspondence between professionals).

The Clinical Record Interactive Search (CRIS) system was established in 2008 to allow researchers access to de-identified EHR data of people accessing SLaM services (Perera et al., 2016). Data are extracted either from structured fields or from free text using natural language processing (NLP) applications developed using General Architecture for Text Engineering (Cunningham, 2002). These applications allow constructs of interest (e.g. symptoms and treatments/interventions) to be ascertained from assessments, letters, and other documents in the EHR (Maudsley Biomedical Research Centre, 2023). The performance of each application is tested prior to being made available.

Study population

The sample comprised adults aged between 21 and 65 years who had an episode of care within SLaM NHS Foundation Trust and received a new diagnosis of ADHD between 1st January 2008 and 8th June 2022. The index date of diagnosis was defined as the date at which a diagnosis of ADHD was first added to a structured field of the EHR with ICD-10 code F90 or where this diagnosis was first recognized by the relevant NLP application. To ensure this was a new diagnosis of ADHD (and not a pre-existing diagnosis that was added to the record in retrospect), we excluded people below the age of 21 years who may have transitioned from child and adolescent mental health services and those who had a record of being prescribed medication used to treat ADHD prior to the ADHD diagnosis index date.

To ensure data integrity, we excluded individuals with very brief episodes of care of ⩽14 days on the basis that such episodes were likely to include only single assessments or inappropriate referrals. Adults over the age of 65 years at the date of diagnosis of ADHD were excluded.

Individuals with intellectual disability were matched to people without intellectual disability in (1:4 ratio) by age at ADHD diagnosis and sex using the MarchIt package in R using the nearest neighbor matching method (Ho, Imai, King, & Stuart, 2011).

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Co-variates

Date of birth, gender, and ethnicity were extracted from the EHR. Age at diagnosis was calculated by subtracting the date of birth from date at which the ADHD diagnosis was added to the EHR. Days in care were defined as the number of days that the individual was under the care of any mental health service provided by SLaM, from the date of first acceptance to the date of discharge, excluding time spent on a wait list.

Clinical diagnoses, recorded at any time during the individual's care episode, were ascertained from structured fields and included schizophrenia and related psychotic disorders (ICD-10 codes F20–F29), bipolar affective disorder (F31), depression (F32, F33), anxiety disorders (F41), obsessive-compulsive disorder (F42), personality disorder (F60, F61), intellectual disability (F70–F79), and pervasive developmental disorder, including autism (F84) (World Health Organization, 1993). Degree of intellectual disability (categorized as mild, moderate, severe, or profound) was obtained from the structured diagnosis field or from free text records.

The symptoms recorded in the EHR in the 12 months preceding the diagnosis of ADHD were assumed to be relevant to the ADHD diagnosis. NLP applications were used to extract a range of symptoms documented in the year prior to the ADHD index diagnosis date, with each being classed as either present (recorded at least once in the EHR) or absent (not recorded). We reviewed the full NLP application dictionary for suitable applications to apply to the data that approximated possible ADHD presenting symptoms as described in major classification systems (American Psychiatric Association, 2013; World Health Organization, 1993) and discussed these with clinicians working in the field.

Medication data were extracted using NLP searches and medication was categorized according to the British National Formulary (BNF) sub-chapter (anti-psychotic, mood stabilizer, anti-depressant, and anxiolytic/hypnotic) (Joint Formulary Committee, 2023) and listed in online Supplementary data Table S1. Medication for ADHD (BNF sub-chapter 4.4) was divided into stimulant medication (dexamfetamine, lisdexamfetamine, and methylphenidate) and non-stimulant medication (atomoxetine, guanfacine, modafinil, and pitolisant). Medication was recorded as being prescribed in the 12 months before the ADHD index diagnosis date (used to exclude known cases and to explore the impact of existing prescriptions on prescribing of medication for ADHD) or in the 12 months after the diagnosis of ADHD.

Statistical analysis

We described data related to demographic characteristics, clinical conditions, symptoms related to ADHD prior to the diagnosis, and medication prescription using descriptive statistics and compared these between adults with and without intellectual disability using Fisher's exact and Mann-Whitney *U* tests.

We then conducted three main analyses. First, logistic regression models, reporting odds ratios (OR), and 95% confidence intervals (95% CI), were fitted to estimate associations between demographic and clinical variables and symptoms of ADHD in adults with intellectual disability compared to controls without intellectual disability. The first model (background model) consisted of age and sex. Ethnicity could not be included in this model due to a high amount of missing data. In the second model (clinical variable model) we adjusted for clinical conditions including autism, bipolar disorder, depression, anxiety disorder, schizophrenia / psychosis, obsessive-compulsive disorder, and personality disorder.

Next, symptoms of ADHD prior to ADHD diagnosis were examined to investigate potential associations between these symptoms and intellectual disability while adjusting for age, sex, and clinical conditions. Symptoms related to ADHD were only included in the regression models if they were present in 10% or more of the sample. Our second analysis investigated factors associated with ADHD medication prescription up to one year after ADHD diagnosis. We followed the same approach described above using logistic regression modeling but with the inclusion of intellectual disability diagnoses as a factor in all models.

Sub-analyses were then conducted to examine the relationship between medication prescription for mental health conditions prior to ADHD diagnosis and their effect on prescription of ADHD medication following the diagnosis using logistic regression models adjusting for age, sex, and the medication of interest (antipsychotics, anxiolytic, antidepressants, and mood stabilizers). We also examined whether being prescribed ADHD medication after the diagnosis of ADHD was related to previous prescriptions of psychotropic drugs using McNemar's Chi-squared test for paired samples. To be eligible for these analyses, people had to have been prescribed the other psychotropic medication type prior to their ADHD medication prescription. We examined medication data up to 365 days after ADHD medication prescription and, due to a limited sample size, we did not differentiate between adults with intellectual disability and general population controls.

Ethical approval

The SLaM BRC case register has overarching ethical approval from the Oxfordshire Research Ethics Committee C (18/SC/0372) for the secondary analysis of de-identified health data. The study was registered with the CRIS oversight committee (reference: 22-016), which includes representation from service users, and ensures that research complies with ethical and legal standards.

Results

A total of 178 adults with intellectual disability were matched to 712 controls. Eighty-three people (19 with intellectual disability and 64 controls) were prescribed ADHD medication prior to the index diagnosis date and were therefore excluded from further analysis due to having an unreliable diagnosis date. The final cohort comprised 159 adults with intellectual disability newly diagnosed with ADHD between January 2007 and June 2022 at, or over, the age of 21 years and below the age of 65 years, and 648 matched controls without intellectual disability (Table 1).

The median duration under secondary mental healthcare services was 687 days (IQR 232-1704 days); people with intellectual disability spent significantly longer under services than those without intellectual disability (933 days *v.* 665.5 days, $p < 0.003$). The median time spent under SLaM services prior to the ADHD diagnosis index date was 12 months. Median age at diagnosis of ADHD was 27 years. Just over half of the cohort were of white ethnicity; a greater proportion in the intellectual disability sample were of Black ethnicity and ethnicity was more likely to be unknown in the general population control group.

Roughly three times as many males as females with intellectual disability were diagnosed with ADHD over the course of the study period. Almost half (46.5%) of those with intellectual disability who were diagnosed with ADHD had a co-occurring diagnosis

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Table 1. Characteristics of adults with intellectual disability and ADHD compared to general population controls with ADHD

	Toal sample ($n = 807$)	Adults with intellectual disability and ADHD ($n = 159$)	General population controls with ADHD ($n = 648$)	p value of comparison between adults with intellectual disability and without intellectual disability
Total days under services (median [IQR])	**687 [232–1704]**	**933 [378–1974.50]**	**665.5 [214.50–1590.50]**	**0.003**
Days under services prior to ADHD diagnosis (median [IQR])	**365 [101.5–364]**	**263 [85.5–364]**	**235.5 [105–364]**	**0.14**
Age at diagnosis (median [IQR])[a]	27.00 [23.00–35.00]	27.00 [23.00–35.00]	27.00 [23.00–34.25]	0.99
Ethnicity, *n* (%)				
Asian	15 (1.9)	5 (3.1)	10 (1.5)	**0.005**
Black	79 (9.8)	41 (25.8)	38 (5.9)	
White	443 (54.9)	82 (51.6)	361 (55.7)	
Mixed and other	59 (7.3)	13 (8.2)	46 (7.1)	
Not stated or unknown	211 (26.1)	18 (11.3)	193 (29.8)	
Gender, *n* (%)[a]				
Female	219 (27.1)	42 (26.4)	177 (27.3)	0.84
Male	588 (72.9)	117 (73.6)	471 (72.7)	
Degree of intellectual disability, *n* (%)				
Mild	–	90	–	–
Moderate	–	27	–	–
Severe	–	17	–	–
Unknown		25		
Pervasive developmental disorder, *n* (%)	**148 (18.3)**	**74 (46.5)**	**74 (11.4)**	**<0.001**
Bipolar affective disorder, *n* (%)	24 (3.0)	7 (4.4)	17 (2.6)	0.29
Depression, *n* (%)	52 (6.4)	10 (6.3)	42 (6.5)	1.00
Schizophrenia/psychosis, *n* (%)	**69 (8.6)**	**37 (23.3)**	**32 (4.9)**	**<0.001**
Anxiety disorder, *n* (%)	34 (4.2)	11 (6.9)	23 (3.5)	0.075
Obsessive compulsive disorder, *n* (%)	10 (1.2)	3 (1.9)	7 (1.1)	0.42
Personality disorder, *n* (%)	**79 (9.8)**	**32 (20.1)**	**47 (7.3)**	**<0.001**
Antipsychotic prescription before diagnosis, *n* (%)	**115 (14.3)**	**68 (42.8)**	**47 (7.3)**	**<0.001**
Hypnotic/anxiolytic prescription before diagnosis, *n* (%)	**96 (11.9)**	**60 (37.7)**	**36 (5.6)**	**<0.001**
Anti-depressant prescription before diagnosis, *n* (%)	**103 (12.8)**	**43 (27.0)**	**60 (9.3)**	**<0.001**
Mood stabilizer prescription before diagnosis, *n* (%)	**67 (8.3)**	**40 (25.2)**	**27 (4.2)**	**<0.001**
Any psychotropic medication	**185 (22.9)**	**96 (60.4)**	**89 (13.7)**	**<0.001**

[a]Matched variables.
Bold text, significant at $p < 0.05$.

of autism compared to 11% of the general population. People with intellectual disability were also significantly more likely to have a diagnosis of schizophrenia and a diagnosis of personality disorder than those without intellectual disability. The intellectual disability group had significantly higher rates of psychotropic medication prescription prior to the diagnosis of ADHD across all major categories of psychotropic drugs.

In the adjusted model (Table 2), people with intellectual disability who were diagnosed with ADHD were more likely than controls without intellectual disability to have been diagnosed with pervasive developmental disorder(OR 5.19, 95%CI 3.22–8.42) and less likely to have been diagnosed with depression (OR 0.33, 95%CI 0.12–0.83) during their time under mental health services.

The most commonly recorded symptoms in the year prior to the ADHD index diagnosis date for both groups were anxiety (symptom), agitation, aggression, and disturbed sleep (online Supplementary data Table S2). All symptoms were more common in people with intellectual disability, with the exception of anergia, which was very seldom reported (online Supplementary data Table S2). Adjusting for potential confounders, people with intellectual disability were more likely to have symptoms of agitation, aggression, hostility, and mood instability, and less likely to have poor concentration recorded in their clinical notes prior to the diagnosis of ADHD than those without intellectual disability (Table 2).

In the year following the diagnosis of ADHD, a significantly smaller proportion of people with intellectual disability than without were prescribed medication to treat ADHD (27.7% with intellectual disability compared with 46.0% without intellectual disability, $p < 0.001$) (Table 3). This difference was largely accounted for by a significantly lower proportion of those with intellectual disability who were prescribed stimulant medication (24.5% with intellectual disability compared with 42.0% without intellectual disability, $p < 0.001$). There was no difference in the proportion prescribed non-stimulant medication for ADHD or those who had received both types of medication in the follow-up window.

Examining the factors associated with any ADHD medication prescription (stimulants and/or non-stimulants; Table 4) up to 1 year after ADHD diagnosis showed that having a diagnosis of intellectual disability was associated with decreased odds of being prescribed ADHD medication (OR 0.60, 95%CI 0.38–0.91). People with diagnoses of schizophrenia and personality disorders were also less likely to be prescribed ADHD medication than those without these conditions (OR 0.27, 95%CI 0.13–0.53, and OR 0.43, 95%CI 0.23–0.76, respectively). Symptoms recorded prior to the ADHD diagnosis were not significantly associated with ADHD medication prescription following the diagnosis (all $p > 0.05$).

As our analysis suggested that certain mental health conditions were associated with a decreased likelihood of being prescribed ADHD medication, we further examined the potential associations between pre-existing medication for mental health conditions and the prescribing of ADHD medication. These sub-analyses (Table 5) were conducted separately for those with and without intellectual disability as there were significant differences in prescription rates for each drug class between the two groups (see Table 1).

In adults with intellectual disability, being prescribed antipsychotic, anxiolytic, and mood stabilizer medications prior to their ADHD diagnosis were all associated with decreased odds of being prescribed ADHD medication post-diagnosis (Table 5). In the general population controls, adults who were prescribed antipsychotic, anti-depressant, and mood stabilizing medications

Table 2. Clinical diagnoses and symptoms associated with adults with intellectual disability and ADHD compared to general population controls with ADHD

Background model				
		95% CI		
	OR	LL	UL	*p* value
Age at diagnosis	1.00	0.98	1.02	0.92
Male sex	1.05	0.71	1.56	0.82
Clinical variables model				
Age at diagnosis	1.00	0.98	1.02	0.99
Male sex	0.96	0.61	1.53	0.87
Pervasive developmental disorder	**7.35**	**4.8**	**11.32**	**<0.001**
Bipolar affective disorder	1.47	0.47	4.16	0.48
Depression	0.58	0.24	1.27	0.19
Anxiety disorder	1.24	0.5	2.94	0.63
Schizophrenia / psychosis	**5.72**	**3.23**	**10.19**	**<0.001**
Obsessive compulsive disorder	0.79	0.13	4.01	0.79
Personality disorder	**3.13**	**1.75**	**5.59**	**<0.001**
Pre-diagnosis symptoms model				
Age at diagnosis	0.99	0.97	1.02	0.62
Male sex	1.11	0.67	1.88	0.70
Pervasive developmental disorder	**5.19**	**3.22**	**8.42**	**<0.001**
Bipolar affective disorder	0.96	0.27	3.01	0.95
Depression	**0.33**	**0.12**	**0.83**	**0.02**
Anxiety disorder	0.99	0.36	2.56	0.98
Schizophrenia / psychosis	1.66	0.78	3.46	0.18
Obsessive compulsive disorder	0.78	0.11	4.35	0.79
Personality disorder	1.02	0.48	2.09	0.96
Agitation	**2.73**	**1.43**	**5.24**	**0.002**
Aggression	**2.86**	**1.56**	**5.25**	**<0.001**
Anxiety (symptom)	1.46	0.83	2.52	0.18
Arousal	1.38	0.50	3.81	0.53
Disturbed sleep	1.73	0.88	3.36	0.11
Elation	1.18	0.42	3.27	0.75
Hostility	**2.65**	**1.10**	**6.45**	**0.03**
Insomnia	0.96	0.40	2.23	0.92
Irritability	0.5	0.21	1.11	0.09
Mood instability	**2.29**	**1.15**	**4.58**	**0.02**
Poor motivation	1.31	0.59	2.86	0.51
Poor concentration	**0.19**	**0.10**	**0.38**	**<0.001**

Bold text, significant at $p < 0.05$.

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Table 3. Medication within 1 year after diagnosis of ADHD

	Total sample	Adults with intellectual disability and ADHD	General population controls with ADHD	*p* value of comparison
Any ADHD medication prescribed in the year following diagnosis (%)	342 (42.4)	44 (27.7)	298 (46.0)	<0.001
Stimulant ADHD medication prescribed in the year following diagnosis (%)	311 (38.5)	39 (24.5)	272 (42.0)	<0.001
Non-stimulant ADHD medication prescribed in the year following diagnosis (%)	51 (6.3)	8 (5.0)	43 (6.6)	0.59
Stimulant *and* non-stimulant ADHD medication prescribed in the year following diagnosis (%)	20 (2.5)	3 (1.9)	17 (2.6)	0.78

Table 4. Factors associated with prescription of any ADHD medication up to 1 year after ADHD diagnosis in adults with intellectual disability and ADHD and general population controls with ADHD

Background model				
		95% CI		
	OR	LL	UL	*p* value
Age at ADHD diagnosis	0.99	0.98	1.01	0.44
Sex (Male)	1.14	0.83	1.57	0.42
Intellectual disability	**0.45**	**0.30**	**0.65**	**<0.001**
Clinical variables model				
Age at ADHD diagnosis	1.00	0.98	1.01	0.80
Sex (Male)	1.04	0.75	1.46	0.81
Intellectual disability	**0.60**	**0.38**	**0.91**	**0.02**
Pervasive developmental disorder	1.03	0.68	1.56	0.89
Bipolar disorder	0.51	0.18	1.28	0.17
Depression	0.63	0.32	1.21	0.18
Anxiety disorder	0.60	0.25	1.34	0.23
Schizophrenia	**0.27**	**0.13**	**0.53**	**<0.001**
Obsessive-compulsive disorder	0.89	0.18	3.51	0.87
Personality disorder	**0.43**	**0.23**	**0.76**	**0.005**
Agitation	1.54	0.92	2.57	0.10
Aggression	0.96	0.57	1.62	0.87
Anxiety (symptom)	1.39	0.91	2.13	0.13
Arousal	0.86	0.34	2.12	0.74
Disturbed sleep	0.79	0.46	1.34	0.38
Elation	0.94	0.35	2.48	0.90
Hostility	0.50	0.19	1.21	0.14
Insomnia	0.50	0.20	1.13	0.11
Irritability	1.02	0.52	1.98	0.96
Mood instability	0.70	0.38	1.27	0.24
Poor motivation	1.00	0.47	2.09	1.00
Poor concentration	1.41	0.87	2.30	0.16

Bold text, significant at $p < 0.05$.

prior to their ADHD diagnosis were all significantly less likely to be prescribed ADHD medication following their diagnosis.

We examined whether being prescribed medication for ADHD following the diagnosis of ADHD was associated with change in existing psychotropic medication prescribing. Owing to small numbers, this analysis used the whole cohort. In people who were prescribed anxiolytic or anti-depressant medication prior to the diagnosis of ADHD, being prescribed medication for ADHD was associated with a significant decrease in prescription of these medications up to one year following the diagnosis of ADHD (online Supplementary data Table S3). There was no association between prescription of medication for ADHD and change in prescription of antipsychotic or mood stabilizing medication.

Discussion

We used real-world data to assemble a large cohort of people with whom ADHD was diagnosed in adulthood. To the best of our knowledge, this is the first study that directly compares the presentation and pharmacological treatment of ADHD between adults with and without intellectual disability and provides clinical insights and evidence of differential treatment provision.

Our sample included over 800 adults who were newly diagnosed with ADHD over a 15-year period. One hundred and fifty-nine of these had a diagnosis of intellectual disability; this group had an average age of diagnosis of just under 30 years and males outnumbered females by almost 3:1. ADHD is more likely to be diagnosed in males than females in both the general population and in those with intellectual disability, with sex ratios of approximately 4:1 commonly reported (Greven, Richards, & Buitelaar, 2018; Perera et al., 2021). A significantly greater proportion in the intellectual disability group in our study was of black ethnicity; this finding is difficult to interpret in due to the high degree of missing ethnicity data in the control group but warrants further investigation as disparities in ADHD diagnosis between ethnic groups in both children and adults have previously been shown (Bergey, Ghiri, Freeman, & Mackie, 2022; Chung et al., 2019).

Those with intellectual disability were more likely to have pervasive developmental disorder (e.g. autism) and a diagnosis of psychosis or personality disorder; this is consistent with existing evidence that highlights increased rates of psychopathology in people with intellectual disability, and in particular psychosis (Cooper, Smiley, Morrison, Williamson, & Allan, 2007; Mazza et al., 2020; Morgan, Leonard, Bourke, & Jablensky, 2008). People with intellectual disability in our sample spent significantly longer under mental health care services, likely indicating

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Table 5. Examining the relationship between medication prescription for mental health conditions prior to ADHD diagnosis and the association with ADHD medication prescription post-diagnosis in adults with intellectual disability and ADHD and general population controls with ADHD

Adults with ID and ADHD					General population adults with ADHD				
Antipsychotic medication prior to ADHD diagnosis					Antipsychotics prior to ADHD diagnosis				
		95% CI					95% CI		
	OR	LL	UL	*p* value		OR	LL	UL	*p* value
Age at ADHD diagnosis	0.98	0.93	1.02	0.27	Age at ADHD diagnosis	1.00	0.98	1.02	0.96
Male sex	2.57	1.03	7.39	0.0565	Male sex	0.99	0.70	1.40	0.94
Antipsychotic prescription before diagnosis	**0.34**	**0.14**	**0.75**	**0.010**	Antipsychotic prescription before diagnosis	**0.42**	**0.21**	**0.80**	**0.01**
Anxiolytic medication prior to ADHD diagnosis					Anxiolytic prior to ADHD diagnosis				
		95% CI					95% CI		
	OR	LL	UL	*p* value		OR	LL	UL	*p* value
Age at ADHD diagnosis	0.97	0.93	1.01	0.15	Age at ADHD diagnosis	1.00	0.98	1.02	0.97
Male sex	2.7	1.09	7.73	0.044	Male sex	0.96	0.68	1.36	0.82
Hypnotic/anxiolytic prescription before diagnosis	**0.35**	**0.14**	**0.78**	**0.013**	Hypnotic/anxiolytic prescription before diagnosis	0.57	0.27	1.14	0.12
Anti-depressant medication prior ADHD diagnosis					Anti-depressants prior to ADHD diagnosis				
		95% CI					95% CI		
	OR	LL	UL	*p* value		OR	LL	UL	*p* value
Age at ADHD diagnosis	0.97	0.92	1.01	0.12	Age at ADHD diagnosis	1.00	0.98	1.02	0.84
Male sex	2.76	1.11	7.95	0.041	Male sex	0.95	0.67	1.35	0.77
Anti-depressant prescription before diagnosis	0.79	0.32	1.85	0.60	Anti-depressant prescription before diagnosis	**0.36**	**0.19**	**0.64**	**<0.001**
Mood stabilizers prior to ADHD diagnosis					Mood stabilizers prior to ADHD diagnosis				
		95% CI					95% CI		
	OR	LL	UL	*p* value		OR	LL	UL	*p* value
Age at ADHD diagnosis	0.97	0.92	1.00	0.10	Age at ADHD diagnosis	1.00	0.98	1.02	0.93
Male sex	2.45	0.98	7.05	0.07	Male sex	0.97	0.68	1.37	0.86
Mood stabilizer prescription before diagnosis	**0.33**	**0.11**	**0.88**	**0.038**	Mood stabilizer prescription before diagnosis	**0.32**	**0.12**	**0.76**	**0.016**

the greater health care need and complexity in this group and possibly some reluctance from primary care providers to take over their management.

We explored psychiatric and behavioral symptoms that clinicians recorded for each person in the 12 months prior to their diagnosis of ADHD, with the assumption that the diagnosis was based on these recorded symptoms. After adjusting for other factors, those with intellectual disability who were diagnosed with ADHD were more likely to display agitation, aggression, and hostility. Such symptoms may commonly be termed 'behavior that challenges' and can reflect undiagnosed mental illness in people who may not understand their symptoms or have difficulty expressing them verbally (Moss et al., 2000). Our findings suggest that behavior that challenges may indicate co-occurring ADHD (Korb, Perera, & Courtenay, 2019; Perera et al., 2021; Perera & Courtenay, 2017). However, behavior that challenges is a non-specific presentation and expert assessment using adapted diagnostic instruments, collateral informant reports, longitudinal monitoring, and pragmatic treatment trials may be necessary to reach a valid diagnosis (Santambrogio, Masi, & Bertelli, 2021). Comparison between people with intellectual disability with and without ADHD may be helpful in elucidating more specific features of ADHD that can help in diagnosis.

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Mood instability was also more common in people with intellectual disability who were diagnosed with ADHD. Mood instability has been recognized as a core component of ADHD but is not part of the diagnostic criteria (Asherson, Buitelaar, Faraoni, & Rohde, 2016) which may mean the presentation is confused with bipolar or personality disorder (Atmaca, Ozler, Topuz, & Goldstein, 2009; Johnson, Morris, & George, 2021). Mood instability may mediate behavioral problems or offending behavior in ADHD (Gudjonsson, Sigurdsson, Adalsteinsson, & Young, 2013; Smith et al., 2022) and is therefore an important treatment target.

People with intellectual disability were less likely to have recorded poor concentration. Poor concentration is generally a subjective symptom and may be less easy to recognize in others. It may be that people with intellectual disability are less able to articulate this symptom or are less likely to be engaged in activities where sustained mental effort is a requirement.

Untreated ADHD is associated with adverse long-term outcomes across a range of domains, including educational, occupational, and social function, substance misuse, accidental harm, and antisocial and offending behavior (Chang, Lichtenstein, D'Onofrio, Sjolander, & Larsson, 2014; Harpin, Mazzone, Raynaid, Kahle, & Hodgkins, 2016; Lindsay et al., 2013; Shaw et al., 2012). Medication for ADHD can be effective in reducing functional impairment and improving quality of life (Coghill, 2010; Faraone, Spencer, Aleardi, Pagano, & Biederman, 2004). In our study, the overall rate of medication treatment for ADHD in the 12 months following the diagnosis was just over 40%, comparable with data from the United States (Zhu, Liu, Li, Wang, & Winterstein, 2018) and raising the possibility of under-treatment, though it is not possible in our study to ascertain reasons why medication may not have been prescribed following the diagnosis.

There were significant differences in the likelihood of receiving medication based on intellectual disability; in the adjusted analysis, people with intellectual disability were less likely than those without intellectual disability to receive medication treatment. There were no significant associations between presenting symptoms and prescription of medication for ADHD. Interestingly, it was not the case that externalizing symptoms (such as outwardly-directed aggression and hostility) predicted medication use although clinicians can feel under pressure to prescribe in cases where behavior is challenging to others (Perry et al., 2018).

There is little comparable information on prescribing rates for ADHD in intellectual disability. One cross-sectional audit in the United Kingdom reported that two-thirds of adults with diagnosed ADHD accessing specialist intellectual disability services were prescribed medication for ADHD, with stimulants being the most commonly prescribed drug type and a substantial minority prescribed non-stimulant medication (Perera et al., 2021). There is evidence that children with intellectual disability and ADHD are less likely to be prescribed stimulants and more likely to be prescribed non-stimulant medication than children with ADHD alone (Osunsanmi & Turk, 2016). However, in our study, the reduced rates of stimulant prescribing were not compensated for by increased non-stimulant prescribing, suggesting possible under-treatment of ADHD in those with intellectual disability.

The lack of a robust formal evidence base for medication treatment of ADHD in adults with intellectual disability may discourage some clinicians from prescribing medication (Royal College of Psychiatrists, 2021). The seeming reluctance to use stimulant medications (methylphenidate and amphetamines) may be due to a higher rate of co-morbidity in people with intellectual disability, including psychosis and physical health conditions such as congenital heart disease, tic disorder, or underweight, that act as relative contra-indications to their use. It may also be that people with intellectual disability are considered less able or less likely to comply with regular monitoring that is advised for these drugs (National Institute for Health and Care Excellence, 2018) and people with intellectual disability have often been assumed to be more susceptible to adverse side-effects of psychotropic medication, perhaps leading to more cautious prescribing. It may also be the case that issues with mental capacity and family and carer views contribute to reduced prescribing in the intellectual disability group.

Our analysis demonstrated that those prescribed psychotropic medication prior to the diagnosis of ADHD were less likely to be prescribed medication for ADHD, though the pattern differs slightly between people with intellectual disability and those without. Clinicians may have been wary of introducing psychotropic polypharmacy and drug-drug interactions or may have considered the existing medication was managing ADHD symptoms. Although limited by relatively small numbers, there was a suggestion that being prescribed ADHD medication following the diagnosis was associated with reduction in the prescription of other psychotropic medications over the following year. Diagnosing and treating ADHD can support the discontinuation of other medications in people with intellectual disability (Korb et al., 2019; Raji & Javaid, 2022), and highlights the importance of thorough assessment and accurate diagnosis in ensuring appropriate treatment.

Strengths and limitations

The strength of this study lies in the use of routine clinical data, gathered over several years and across a number of different clinical teams and by multiple clinicians, to provide detailed insights into how ADHD is diagnosed and treated in adults with intellectual disability, a hitherto under-researched group.

The study has some limitations. The SLaM catchment area is socio-economically and culturally diverse though may not be representative of other areas in the United Kingdom. We used existing NLP applications to explore the presenting characteristics of ADHD in adults; these were not specifically designed to capture ADHD presentations and it is possible that some relevant signs and symptoms were not measured. We have assumed that the symptoms recorded in the clinical notes up to a year prior to the diagnosis of ADHD were relevant to the diagnosis but are not able to say with certainty on what basis the clinician made the diagnosis of ADHD; such work would require additional data collection. We took steps to ensure the ADHD diagnosis index date was accurate, however, it may be that some of these diagnoses were pre-existing diagnoses added to the EHR in retrospect; this may have reduced the sensitivity of discerning symptoms related to the diagnosis of ADHD. Some people may have obtained medication from alternative sources, in which case our data would under-estimate prescribing rates, though we consider this is unlikely as medication for ADHD can only be started and titrated to a stable daily dose by a specialist clinician. We were not able to provide information on the reasons why medication was not prescribed and we did not have a measure of non-pharmacological interventions for ADHD, such as cognitive

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behavioral therapy. A comparator group with intellectual disability without ADHD was not included; this means it has not been possible to compare rates of symptoms between those with ID and ADHD and those with ID alone.

Implications

These findings have several clinical and research implications. That the intellectual disability group have greater rates of diagnosed mental illness and pharmacological treatment in addition to ADHD may reflect earlier misdiagnosis or the increased rate of psychopathology in this group; in either case, the finding underscores the need for specialist clinicians who have training and experience in assessment of adults with intellectual disability to manage complexity, suitably adapt diagnostic criteria, and oversee appropriate treatment for this group.

More work is needed to gain a nuanced understanding of how ADHD presents in adults with intellectual disability. This could be achieved by developing, training, and validating additional NLP applications with a wider range of signs and symptoms that can be applied to future healthcare datasets covering a greater geographic area. Adding a comparator group of adults with intellectual disability without ADHD to the analysis would enable us to test whether the differential rates of certain behavioral symptoms observed between those with and without intellectual disability were attributable to the intellectual disability alone, rather than ADHD in this population. It would be interesting to investigate whether increases in diagnosis of ADHD observed in the general population over time have been mirrored in those with intellectual disability, and further work is needed to explore the effect of sex and ethnicity on diagnosis and treatment.

Greater evidence is needed on the safety and efficacy of medication used to treat ADHD in adults with intellectual disability. Research with EHRs provides a possible option for this, in addition to traditional clinical trials which are costly and may not be a feasible option. Future observational studies could explore the trajectory of psychotropic medication prescribing over time and whether a diagnosis of ADHD influences this, as the initial data in our study have suggested.

Conclusions

This study indicates that ADHD might present differently in adults with intellectual disability compared to adults without intellectual disability, and ADHD appears to be more likely to be diagnosed on the basis of non-specific symptoms and behavior that challenges. Appropriate treatment of ADHD is important to optimize health and social outcomes and reduce disability. We need to understand why adults with intellectual disability who are diagnosed with ADHD are less likely to receive pharmacotherapy and to avoid propagating inequities in care.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291724001338

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Competing interests. All authors declare no competing interests.

Data access. Data are owned by a third party, Maudsley Biomedical Research Centre (BRC) Clinical Records Interactive Search (CRIS) tool, which provides access to anonymized data derived from SLaM electronic medical records. These data can only be accessed by permitted individuals from within a secure firewall (i.e. the data cannot be sent elsewhere), in the same manner as the authors. For more information please contact: cris.administrator@slam.nhs.uk

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