

ADHD and Autism Spectrum Disorder (ASD) in Childhood: establishing the feasibility and validity of a nation-wide e-cohort

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Ethical approval: This study was approved by the NHS Wales Research Ethics Committee (14/WA/0157). Access to data from the SAIL databank was approved by the Information Governance Review Panel (IGRP) (project number 0712). Patient consent is not required for publication.

Data availability statement:

Data within this study are available in the SAIL Databank. Access to the SAIL Databank is subject to review by and independent Information Governance Review Panel (IGRP). The IGRP gives careful consideration to each project to ensure proper and appropriate use of SAIL data, and approval from the IGRP is necessary to access any data. Once access has been granted, it is gained through the SAIL Gateway: a privacy protecting safe haven and remote access system. Details on how to access data from the SAIL Databank is available here: <https://saildatabank.com/data/>.

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Abstract:

Objectives: We investigated the feasibility and validity of establishing a nationwide e-cohort of individuals with a diagnosis of ADHD and/or ASD for future longitudinal research.

Design: Individuals with a childhood diagnosis of ADHD/ASD as recorded on routinely available healthcare datasets were compared with matched controls and a sample of directly assessed individuals with ADHD.

Setting: This study utilised data from the Welsh Secure Anonymised Information Linkage (SAIL) Databank in Wales, UK. Routinely collected data from primary care, Emergency Department and hospital admissions were linked at person level.

Participants: All individuals in Wales, UK born between 01/01/1991 and 31/12/2000. Individuals with a recorded diagnosis of ADHD and/or ASD by age 18 years were identified using ICD-10 and NHS Read codes and matched to three controls each and 154 individuals with ADHD recruited from an established research study.

Outcome measures: Recorded service use for anxiety and depression, alcohol and drug use and self-harm including Emergency Department use in young adulthood (age 16 years to 25).

Results: 7726 individuals had a recorded diagnosis of ADHD (80% male) and 5001 of ASD (79% male); 1.4% and 0.9% of the population respectively. Cox's regression analyses showed ADHD was associated with increased risks of anxiety/depression (HR:2.36, 95% CI:2.20,2.53), self-harm (HR:5.70, 95% CI:5.07,6.40), alcohol (HR:3.95, 95%CI:3.42,4.56), drug use (HR:5.88, 95%CI:5.08,6.80) and Emergency department service use (HR:1.36, 95%CI:1.31,1.41). Those with ASD were at increased risk of anxiety/depression (HR:2.11, 95%CI: 1.91,2.34), self-harm (HR:2.93, 95%CI: 2.45,3.50) and drug use (HR:2.21, 95%CI: 1.66,2.95) but not alcohol use. The ADHD e-cohort were similar to the directly assessed cohort.

Conclusions: Our identification strategy demonstrated the feasibility of establishing a large e-cohort of those with ADHD/ASD with expected patterns of poorer early adult outcomes, demonstrating a valid method of identifying large samples for future longitudinal studies without selective attrition.

Article summary:

Strengths and limitations of this study:

- This study used population wide administrative data from a well-established and comprehensive databank
- Data from both primary and secondary care was combined
- The study utilised a directly assessed sample of those with ADHD to help validate the establishment of the administratively identified sample
- Not all individuals had passed through the whole follow up period at the end of the study
- Studies utilising administrative data is dependent upon that data having been collected and recorded.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) are neurodevelopmental conditions that typically onset in early childhood[1]. These conditions are known to be associated with multiple adverse outcomes[2–4]. One barrier to conducting longitudinal studies of neurodevelopmental and mental health disorders is selective attrition. Multiple studies have observed that individuals with mental health problems, with higher genetic loading for psychiatric disorders[5,6] and from socially disadvantaged backgrounds[7] are more likely to drop out of longitudinal research, potentially limiting generalisability of results, particularly to more severe cases. An alternative approach is to take advantage of routinely collected health care data.

Wales, one of four UK nations with a population of around 3 million, hosts one of the most comprehensive anonymised record-linked data bases, SAIL (Secure Anonymised Information Linkage) Databank (www.saildatabank.com) that includes health and social care data on every individual. These records include not only secondary care, Emergency Department contacts and prescription data but also uniquely encompass primary care and household level data. The aim of this study was to assess the feasibility of identifying those with a diagnosis of ADHD or ASD in childhood using record-linked routinely available healthcare data and investigate the validity of a nationwide e-cohort for future longitudinal clinical, health services, epidemiological and social sciences research. To achieve this aim, we first identified individuals with a childhood record of ADHD and/or ASD using the SAIL record-linked databases and compared them to matched controls for known early adult outcomes (aged 16–25) associated with ADHD and ASD. For those with ADHD we also compared the e-cohort to a hybrid cohort of individuals with known ADHD diagnoses verified by direct interview.

Methods:

Study design and participants:

The SAIL Databank is an electronic resource holding anonymised person-level linkable routinely collected data from health and public settings for individuals in Wales, UK[8]. Each individual is assigned an anonymous linkage field which can then be used to identify their records across different datasets. This system is secure and anonymous, using a privacy-protecting split-file approach. In this study, we utilized the following datasets: the Welsh Demographic Service; the General Practice Database (covering 77%, i.e. 333/432, of all general practices in Wales); the Emergency Department Data Set for NHS Wales; and the Patient Episode Database for Wales (with hospital admissions data for both inpatient and day cases). Full details in Supplementary Table s1.

Individuals with ADHD or ASD in SAIL

We identified a list of codes from the International Classification of Diseases, 10th Revision (ICD-10) associated with ADHD and ASD from published literature and cross mapped them to Read Codes, a coded thesaurus of clinical terms utilised in the UK National Health Service. We prepared an initial list of READ Codes (diagnoses, medications and administrative codes) and ICD-10 codes was shared with General Practitioners and Mental Health clinicians to ensure completeness. This resulted in the identification of additional codes which were added.

Individuals with an ICD-10 or Read Code from the described list recorded in their GP and/or hospital admission data were identified as having ADHD and/or ASD. The first occurrence of these codes was identified and denoted as age at first available diagnosis. Validation of ADHD codes was also undertaken (see record linkage and validation in supplementary methods). No nested directly assessed ASD cohort was available to verify the codes used. A full list of the codes utilised can be seen in supplementary Table s2 whilst a flowchart of the datasets utilised and the number of participants at each stage can be seen in supplementary Figure s1 and s2.

The final sample included all individuals born between 01/01/1991 and 31/12/2000 to enable investigation of early adult outcomes during the study period 01/01/2020 to 31/12/2016. For each individual, the follow up period was defined as their 16th birthday or start of the study period (01/01/2000), whichever came last, to their 25th birthday, end of the study period (31/12/2016), loss to follow up or death, whichever came first.

Additional participants

Population comparison group: To establish prevalence rates of ADHD and ASD diagnoses in childhood, all individuals within the SAIL databank, (representing the population of Wales) born 01/01/1991-31/12/2000 were identified (n=553,551 individuals) and followed to their 18th birthday.

Matched-control sample: Three controls for each ADHD/ASD participant were identified. Controls were matched on week of birth (± 1 year) and sex, inversely matched by ADHD/ASD diagnosis (i.e. controls of cases with ADHD/ASD diagnosed did not have an ADHD/ASD diagnosis), and required to have as much follow up data as the cases they were matched with. To maximize the quality of ADHD/ASD incidence data in controls used during matching, controls with more data coverage before the age of 18 were selected first.

Directly assessed ADHD sample: For comparisons between the electronic cohort and known individuals with ADHD, 579 participants who were given a diagnosis of ADHD using a face-to-face validated diagnostic interview (the Child and Adolescent Psychiatric Assessment)[9] and questionnaire assessments as part of a previous ADHD research study[10] were invited to consent (6-16 years after initial study participation) for their original research data to be anonymously linked to the SAIL databank. All those contacted had been living in Wales at the time of their assessment. All participants had been originally referred into the study by either a Community Paediatric or Child and Adolescent Mental Health Services and had either newly received a diagnosis of ADHD or were

suspected as having a diagnosis. 46% of participants (n=264) consented to data linkage. Written informed consent was obtained from all young people aged 16 and over, assent from those under 16 and from the parents of those aged 16 years or younger. Participant name, date of birth, address at time of initial research assessment and sex were shared with the NHS Wales informatics service and anonymously linked to the SAIL databank.

Outcome measures and covariates:

Anxiety/depression: To assess presence of anxiety and depression disorders, a previously validated common mental health disorders (CMD) measure[11] was utilised. This measure used an algorithm to identify all GP or hospital recordings of anxiety or depression disorders and has been shown to have strong positive and negative predictive validity[11].

Self-harm: All recorded incidents of self-harm were obtained from general practice, Emergency Department and hospital records. As previously described[12,13], this included any recorded non-fatal intentional self-harm including self-injury, self-poisoning and suicidal attempts but not suicidal thoughts, regardless of motivation.

Alcohol use: Alcohol use information was obtained from general practice, hospital (inpatient and out-patient) and Emergency department datasets, as in[13]. This included recorded incidents of harmful use or dependence syndrome as well as alcohol recorded as being involved in a hospital admission.

Drug use: As detailed in[13], drug use information was obtained from general practice, hospital (inpatient and outpatient) and Emergency department datasets. This consisted of records of any

psychoactive substance use diagnoses (except alcohol or tobacco), including harmful use and dependence.

Emergency Department usage: All recorded contacts with hospital Emergency Departments were obtained from the Emergency department dataset.

For anxiety/depression, self-harm, alcohol and drug use measures, records from general practice, Emergency department and hospital in-patient were combined to obtain an overall measure of any occurrence. ICD-10 and Read Codes used for each outcome can be found in their respective cited references.

Any primary care or hospital use: To investigate whether individuals with ADHD or ASD were more likely to present with the above outcomes at primary care or hospital services (including Emergency Department use), occurrences of any of the listed outcomes recorded in the General Practice Database were considered as primary care use, whilst any recorded in the Patient Episode Database for Wales or the Emergency Department Dataset were considered to be hospital use. These were dichotomised into the presence of any outcome or not. Additional analysis looked at the presence of self-harm separately in general practice and hospital records.

Covariates:

Sex and Deprivation data were obtained from the Welsh Demographic Service dataset. Deprivation was assessed using the Welsh Index of Multiple Deprivation (WIMD) obtained for each individual at the start of the follow up period. The WIMD provides a measure of deprivation by small geographical areas (Lower Super Output Areas) based on 7 domains including average income, education, employment and health statistics for individuals in that area. Using the national WIMD cut-offs, quintiles (1 to 5) of deprivation were defined with level 5 representing the most deprived areas.

The age of each participant at the end of the follow-up period was also recorded to control for the variation in dates of birth and therefore length of follow-up.

Data analysis:

To assess population prevalence, the number of individuals with recorded diagnoses of ADHD and/or ASD was identified within the population comparison sample. This was done separately for males and females.

Comparison to controls

As the study focused on individuals diagnosed with ADHD or ASD in childhood, individuals with a first recorded diagnosis after the age of 18 years and their matched controls were removed from the dataset.

Cox's regression analyses were undertaken to compare the risk of having a recorded incidence of each outcome for those with ADHD/ASD compared to matched controls, with age at end of follow up as the time variable and presence/absence of ADHD/ASD as the status variable. Following unadjusted analyses, a second model controlled for sex and proportion of available records and a final model additionally controlled for deprivation.

Cox's regression analyses were also undertaken as sensitivity analyses to investigate risk of early adult outcomes for those with ADHD/ASD and matched controls stratified by sex and separately by deprivation quintile.

Binomial regression analysis was undertaken to investigate whether, in those with recorded self-harm or Accident and Emergency department usage, the number of incidents of self-harm and Emergency department visits was greater in those with ADHD/ASD compared to matched controls. These models were controlled for sex, age at end of follow up, proportion of available records and deprivation index.

As the SAIL databank maintains records only from Welsh organisations, individuals who move outside of Wales (and back) or to GP practices not covered by the SAIL databank may not have complete follow up data. Therefore, analyses were repeated excluding those with <98% total data coverage.

Results:

For a flowchart of the databases utilised and the number of participants utilised at each stage, see supplementary Figure S2. Average coverage of the datasets was comparable with other cohorts (e.g. [13]) with 99.4% coverage from PEDW and 65.2% average coverage of GPD of the time prior to 18 years.

Identification of ADHD and ASD diagnoses and prevalence

Within the e-cohort, a total of 7726 individuals had a recorded diagnosis of ADHD and 5001 of ASD by the age of 18 years (see table 1). This represents 1.4% and 0.9% of the total Welsh population within that age group. 0.2% (n=1157) had both ADHD and ASD with 22.5% of all individuals with ADHD having a comorbid diagnosis of ASD and 15.3% of all individuals with ASD having a comorbid diagnosis of ADHD. Males were more likely than females to have a diagnosis of ADHD with 2.2% of

males and 0.6% of females receiving such a diagnosis. The same pattern was observed for those with ASD with 1.5% of males and 0.4% of females receiving such a diagnosis.

Comparison between those with ADHD and matched controls:

A total of 19,532 individuals were identified as matched controls for ADHD individuals. Whilst matched on age and sex, those with ADHD came from slightly more deprived backgrounds than their matched controls (see Table2). The mean age at diagnosis for those with ADHD was 9.87 years (sd: 3.81). A summary of the associations between ADHD and outcomes can be seen in Figure 1. Controlling for age, those with ADHD had approximately a two-fold increase in risk of having a record of anxiety or depression (HR:2.36, 95%CI:2.20, 2.53) and a five-fold increase in risk of self-harm (HR:5.70, 95%CI:5.07, 6.40). They were significantly more likely to have a record of alcohol (HR:3.95, 95%CI:3.42, 4.56) and drug use (HR:5.88, 95%CI: 5.08, 6.80) and were more likely to have used Emergency Department services (HR:1.36, 95%CI:1.31, 1.41). All associations remained when controlling for sex, record availability and deprivation (supplementary table s3). For those with recorded self-harm or Emergency Department visits, those with ADHD had significantly more frequent visits than controls (Supplementary table s4). Increased risk of self-harm was observed using both GP (HR:6.5, 95%CI:5.65, 7.72) and hospital records (HR:7.07, 95%CI:5.91, 8.48) (supplementary table s5). When stratifying the outcomes by sex, both males and females were at higher risk for all outcomes and there was generally no difference in the magnitude of this risk, except that females with ADHD were more likely to utilise Emergency Department and hospital services than males with ADHD. (figure 2 and supplementary tables s6 and s7). Similarly, there were no clear differences in the magnitude of risks by level of deprivation (supplementary figure s3 and table s8). When those with incomplete data coverage were removed from the analyses (n=1696, 6.4%), there were no changes in the findings (supplementary table s9).

Comparison between those with ASD and matched controls:

A total of 11,427 individuals were identified as matched controls for the 5001 individuals with ASD. Those with ASD came from similar deprivation backgrounds as their matched controls (see Table 2). The mean age of diagnosis for ASD was 10.02 years (sd:4.52). A summary of the difference between the prevalence of the early adult outcomes between these two groups can be seen in Figure 1. Those with ASD had approximately a two-fold risk of having a record of anxiety/depression (HR:2.11, 95%CI:1.91, 2.34) and were almost three times more likely to have a record of self-harm (HR:2.93, 95%CI:2.45, 3.50). They were more likely to have a record of drug use (HR:2.21, 95%CI: 1.66,2.95) but showed similar levels of alcohol use problems (HR:1.19, 95%CI:0.91, 1.55) and rates of Emergency Department use (HR:0.95, 95%CI:0.90, 1.00) (see figure 1 and Table 2). Associations remained robust controlling for sex, record availability and deprivation (see supplementary Table s10). An ASD diagnosis was associated with slightly reduced self-harm; however for in those who self-harmed, those with ASD were more likely to have repeated self-harm than controls. Increased risk of self-harm was observed in GP (HR:3.60, 95% CI:2.86, 4.53) and hospital records (HR:3.75, 95% CI:2.85, 4.93) (see supplementary table s11). For those who utilised Emergency Department care, those with ASD had significantly more visits than their matched controls (Supplementary table s4). As seen in figure 3 and supplementary tables s12 and s13, findings were similar for males and females and, in general there were no differences in the risks across sex. The exception to this was that females with ASD were more likely to utilise Emergency Department and hospital services than males with ASD. When stratified by deprivation (table s14 and figure s4), there was no clear differences in the findings by deprivation. When those with incomplete coverage were removed from the analyses (n=1004, 6.4%), the findings remained the same (supplementary table s15).

Comparison of directly assessed ADHD sample to those identified in the e-cohort:

Within the directly assessed sample, 154 individuals who were born between 1991 and 2000 and were included in the matched sample dataset. The directly assessed ADHD cohort were younger at the end of follow up than those in the e-cohort only (mean:19.11 years, sd:2.20 vs mean:21.20 years, sd:3.80; $t=11.320$, $p<0.001$) and had an earlier age at ADHD diagnosis (mean:8.41 years, sd:3.34 vs mean:10.54 years, sd:3.86; $t=7.949$ $p<0.001$). There groups were similar on other demographic measures (Supplementary table s16). The difference in age at diagnosis remained when controlling for age, sex, proportion of follow-up records and deprivation (Unst. Beta:-1.342, 95%CI:-1.91, -0.774, Beta=-0.045). When controlling for length of follow up, there were no significant differences between those in the hybrid and e-cohort for all outcome measures.

Discussion:

The aims of this study were to establish and validate a nationwide e-cohort of young people in Wales with recorded diagnoses of ADHD and/or ASD. These aims were successfully achieved; lists of relevant ICD-10 and NHS Read codes were created and utilised to identify an e-cohort of individuals with ADHD and/or ASD. In comparisons between these groups and matched population controls we observed associations of ADHD or ASD with adverse early adult outcomes in-line with research findings from the UK and other countries, validating the identification strategy[2,3,14–17]. Further validating the process, those with ADHD in the e-cohort were compared to a hybrid cohort of individuals with known ADHD diagnoses. These groups did not differ in their early adult outcomes and were demographically similar, apart from that those in the hybrid cohort were younger and had an earlier age at diagnosis. The identification of diagnosed individuals utilised data from multiple databases (General Practice, hospital and prescription records) which reinforces presumed assumptions that there is no single code or database routinely used for recording for ADHD or ASD diagnoses within Wales (and the UK). This is in contrast to the national registries in some other countries, such as Sweden and Denmark where diagnoses are routinely recorded using ICD and

standardised prescription codes (e.g.[18,19]). In the UK (as in some other countries), diagnoses of ADHD and ASD are made by specialists and not by primary care but ICD codes are not always used.

The administrative prevalence of individuals with a recorded diagnosis of ADHD and ASD (1.4% and 0.9% of the respectively) in Wales, identified in the SAIL databank corresponds well with the population prevalence of these disorders from the largest, recent UK epidemiological survey: the 2017 Mental Health of Children and Young People survey[20] which directly assessed a representative sample of 5-19 year olds in England (not Wales) using the Development and Wellbeing Assessment, a structured diagnostic interview[21]. Rates of DSM-5 diagnoses reported in that study were 1.6% for ADHD and 1.2% for ASD. The rate of ADHD in that survey is much lower than the rates reported in meta-analyses of ADHD which suggest global prevalence rates of around 5 to 7% with variation explained by methodological differences across study rather than because of substantial differences between countries[22]. This may explain why an earlier English mental health population survey[23] observed a prevalence rate of 2.4% for DSM-IV defined ADHD. Population prevalence rates for ADHD symptom levels do not appear to have changed over time[22,24]. Administrative rates of ADHD have varied considerably across time and different countries with the UK and Scandinavian countries generally showing a rate commensurate with or lower than the population prevalence rate[25,26] while some American States show very high administrative prevalence rates[27].

In contrast, population rates of autism have increased over time[28]. This is thought to be mainly attributable to changes in diagnostic criteria and methods of assessment[29]. However the population rate of autism in 2005 in England (0.9%) is[30] similar to that reported in the most recent 2017 survey[20]. The prevalence rates for males and females with an excess of males affected in our study are in line with population and administrative surveys[31,32]. A recent study looking at rates of Autism also using the SAIL databank, using similar methodology, found a slightly lower prevalence

rate than in this study (0.5%)[33]. However, this difference is likely to be due to the age range of the sample and the known increase in diagnostic prevalence over time as that study looked at individuals with autism at any age, whilst we restricted to a diagnosis before the age of 18 years.

Our study investigated diagnoses recorded in healthcare. If we use findings from the 2017 England population survey, this suggests that there is neither an over or under diagnosis of ADHD or ASD in Wales. However, using data from other surveys would suggest that there could be under-diagnosis of ADHD but that administrative ASD rates are in line with nearly all population surveys. In this study we also identified those with both ADHD and ASD despite co-diagnosis being disallowed by ICD and DSM until recently; these are findings that are also observed in the Danish registry (e.g.[34]). This suggests that clinicians, unlike researchers, are more willing to dispense with diagnostic rules. However, it is possible that future estimates of ADHD and ASD co-diagnosis will be higher since DSM-5 and ICD-11 no longer disallow this[35]. Looking at adverse outcomes in early adulthood, ADHD was significantly associated with all the outcomes studied. Perhaps most strikingly, there was more than a five-fold increased risk of self-harm in individuals in this group, whilst we also observed that, of those with recorded self-harm events, those with ADHD had an increased number of incidents. Whilst this increased risk of self-harm in those with ADHD has previously been reported (e.g.[36], especially when looking specifically at suicidal behaviour), our study extends previous studies as it includes self-harm behaviours recorded in primary as well as secondary care.

A recorded diagnosis of ASD was associated with increased risk of anxiety/depression, self-harm and drug use. Again, these are in line with previous literature[17,37,38], thereby validating findings from this e-cohort. Interestingly, those with ASD showed similar levels of alcohol use problems and Emergency department use for those with ASD, although of those who did have contact with Emergency departments, had more visits than their matched controls. Whilst an increased risk was observed for those with ADHD or ASD across a range of adverse outcomes, this risk tended to be

greater for those with ADHD for all outcomes except anxiety/depression where there was an equally increased risk.

Sensitivity analyses suggests that adverse outcomes for ADHD and ASD are similar in males and females and across economic/deprivation strata. Comparisons of the sample of individuals with a diagnosis of ADHD confirmed by research diagnostic interviews who consented to record linkage and the generated e-cohort demonstrated that they were generally similar, although individuals within the hybrid cohort were younger at the end of the follow up period and were also likely to be younger at age of diagnosis. As participants were part of a larger research study who were re-contacted to request consent for data linkage, the reduced follow up period, indicating a younger hybrid cohort, may reflect the difficulties of continued contact with research participants as they move into adulthood. This highlights the difficulties of longitudinal follow up studies, further demonstrating the benefits of linking routinely collected health data for assessing longer term outcomes. When the length of follow up was taken into consideration, individuals with ADHD in the hybrid and e-cohort were similar, indicating that the e-cohort successfully identified individuals reflective of those with ADHD in the Welsh population.

This study demonstrates that health record data for a whole nation via the SAIL Databank can be used to identify those with a diagnosis of ADHD and ASD and enabling (anonymous) longitudinal follow up for all individuals still living in Wales, reducing issues associated with selective attrition that can be a disadvantage for longitudinal cohort studies[5–7]. By looking at the population level, we have a large sample of individuals with ADHD/ASD and so can look at a range of outcomes including those which are less common, such as drug and alcohol use. Our study also highlights the opportunity for other types of large-scale studies including examining early risk factors, service use,

physical health, educational and social outcomes (via linkage with education and social care records in Wales).

The verification of ADHD codes using a directly assessed sample as comparison was successful and gives confidence that the e-cohort is similar to those with a known diagnosis. However, there are limitations. This verification process could have been improved by including a directly assessed sample without ADHD to assess the false positive rate, however this was not available. Similarly, verification of the ASD codes would have been advantageous. However, identifying a sample of individuals of similar prevalence to the most recent population survey in England[20] and the observed association of ASD with adverse early adult outcomes increases confidence in our identification methods.

Whilst using a good set of verified codes, as with any data linkage study, we were reliant upon the information recorded in the relevant dataset. Therefore, individuals whose ADHD/ASD has not been assessed or diagnosed clinically or where such diagnoses were not accurately recorded would not be included in our sample. This may also be the case for the outcome measures; although we used previously established methods to identify these, if they are not recorded (e.g. self-harm not reported to health care services, and the known underestimation of community alcohol and drug use) they would not be represented in our sample. It is also the case that the follow up period differed between individuals and was not long for the youngest in our cohort, thus potentially underestimating the prevalence of the outcomes. It is worth noting that these limitations are relevant to the matched controls as well as the individuals with recorded ADHD/ASD diagnoses and that the unique availability of records from both primary and secondary care in the SAIL databank may mitigate reporting issues.

Another limitation is that we also restricted the sample to those with a diagnosis of ADHD/ASD by age 18 years, as we were interested in what happens to those with a childhood diagnosis as they grow older. However, we know that many individuals are diagnosed with ADHD and ASD in adulthood (especially females) and investigating their difficulties, especially in comparison to those with a childhood diagnosis, would be interesting.

Overall, this study has demonstrated the feasibility and validity of an e-cohort of those with ADHD and ASD using health record-linked data in Wales, UK. Our identification strategy resulted in a large sample who could be followed longitudinally into early adulthood with minimal attrition. This type of cohort can be utilised in future studies, benefitting from the linkage of information from primary and secondary healthcare, social care and educational data available via the SAIL databank, to further understand the risks and outcomes for those with ADHD and ASD as well as to support planning in health and social care services.

Author contributions:

Concept and design: KL, AJ, SP, AT. Acquisition, analysis or interpretation of data: KL, MDPB, SD, SP, LR, AJ, AT. Drafting of the manuscript: KL, MDPB, AT. Statistical analysis: KL, MDPB, Critical revision of the manuscript for important intellectual content: KL, MDPB, SD, SP, LG, AJ, AT. KL and MDPB had access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. KL is the guarantor.

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Table 1: Overall prevalence of ADHD and ASD, diagnosed in childhood

	ADHD*	ASD*	ADHD and ASD	No Diagnosis
Overall	7726 (1.4%)	5000 (0.9%)	1157 (0.2%)	541, 982 (97.9%)
Males**	6213 (80%)	3941 (79%)	978 (85%)	268,066 (49%)
Females**	1513 (20%)	1059 (21%)	179 (15%)	273,913 (51%)
Deprivation:***				
WIMD Quintile: 1	839 (11%)	756 (15%)	156 (13%)	102,867 (20%)
WIMD Quintile: 2	1019 (13%)	788 (16%)	163 (14%)	98,336 (19%)
WIMD Quintile: 3	1325 (17%)	948 (19%)	213 (18%)	93,378 (17%)
WIMD Quintile: 4	1710 (22%)	1174 (24%)	260 (23%)	99,687 (18%)
WIMD Quintile: 5	2833 (37%)	1329 (27%)	365 (32%)	112,861 (21%)

* Including those with comorbid ADHD and ASD

** A number of individuals n<5 (all with no diagnosis) had missing data on sex

*** n=34,858 individuals (n=34,853 with no diagnosis and n=5 with ASD) had missing deprivation data

Table 2: Summary of demographics and adult outcomes for ADHD and ASD cases and controls:

	ADHD Controls	ADHD Cases	ASD Controls	ASD Cases
N	19,532	7738	11,427	5001
Male gender	15,568 (79.7%)	6223 (80.4%)	8817 (77.2%)	3945 (78.9%)
Age at end of follow up (GP records): Mean (sd)	20.4 (2.8)	19.97 (2.7)	19.6 (2.8)	19.4 (2.6)
Deprivation index quintile (start of follow up): Mean (sd)	3.2 (1.5)	3.4 (1.4)	3.1 (1.4)	3.2 (1.4)
Age at ADHD diagnosis: Mean (sd)	-	9.8 (3.8)	-	8.9 (4.2)
Age at ASD diagnosis: Mean (sd)	-	10.3 (4.9)	-	10.0 (4.5)
Anxiety or depression: N (%)	1879 (9.6%)	1324 (17.1%)	919 (8.0%)	653 (13.1%)
Drug use - any: N (%)	284 (1.5%)	497 (6.4%)	110 (1.0%)	80 (1.6%)
Alcohol use – any: N (%)	349 (1.8%)	408 (5.3%)	192 (1.7%)	76 (1.5%)
Self-harm – any: N (%)	447 (2.3%)	769 (9.9%)	243 (2.1%)	241 (4.8%)
Self-harm – number of recorded incidents: Mean (sd)	0.04 (0.37)	0.28 (1.41)	0.04 (0.37)	0.16 (1.29)
Emergency Department use – any: N (%)	10,550 (54%)	4899 (62%)	5668 (50%)	2115 (42.3%)
Emergency Department use – number of recorded visits: Mean (sd)	1.67 (2.61)	3.07 (6.19)	1.45 (2.57)	1.54 (3.95)

Figure 1: Associations between ADHD and ASD with early adult outcomes

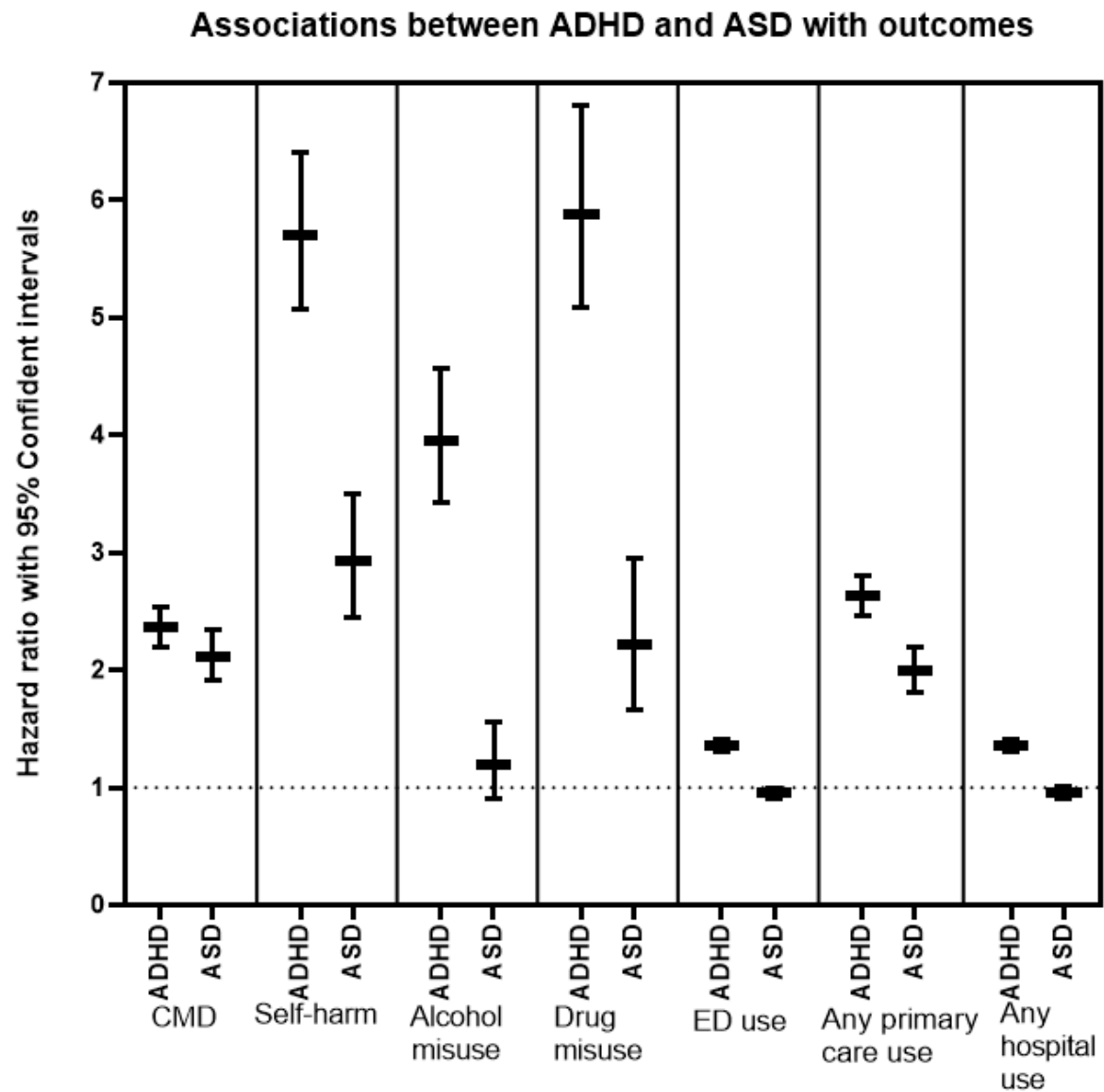


Figure 2: Associations between ADHD and early adult outcomes, by sex

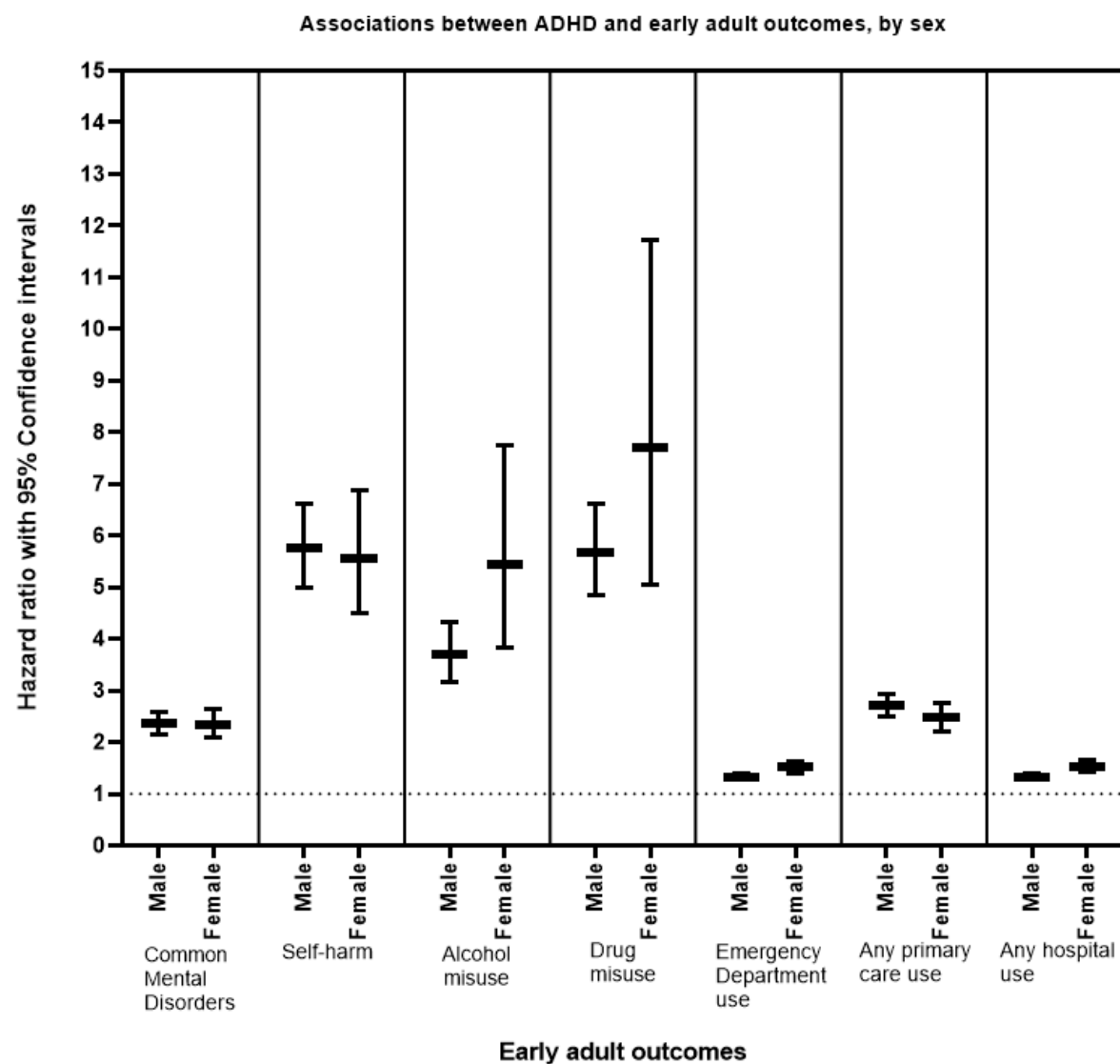


Figure 3: Associations between ASD and early adult outcomes, by sex

