Evaluating the misdiagnosis of ADD in patients with prior history of depression: A claims data study in Germany

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Background

Attention Deficit Disorder (ADD) with or without hyperactivity is one of the most frequent neurodevelopmental disorders in children with a persistence rate into adulthood varying between 40 and 50% [1]. Additionally, in Germany, the prevalence rate of ADD in adults is approximately 4.7% [2].

Studies show prevalence rates of ADD for adult females are higher than for girls which indicates underdiagnosed of ADD in girls [3]. With depression being one of the most frequent comorbidities of ADD with a prevalence of 35-70% [4], literature highlights that ADD is oftentimes misdiagnosed as depression and it can especially be seen in females due to the overlapping symptoms and the tools used to diagnose ADD in children and adults [5].

However, there has been no real-world evidence studies conducted in Germany to test this hypothesis.

Thus, the objective of this study was to estimate the incidence rate of ADD in females and males previously diagnosed with depression, as well as to determine factors associated with the potential misdiagnosis.

Methods

This study utilized claims data from a German sickness fund (AOK PLUS), covering the study period of 1/1/2015-30/6/2021. In order to be included in the study population the following inclusion criteria must have been met:

- 1. At least 1 inpatient or outpatient confirmed or suspected diagnosis of depression (ICD-10 GM code: F32 or F33) by a specialist (i.e. psychiatrist or psychotherapist) from 1/1/2016 until 30/6/2021
- 2. No confirmed ADD (ICD-10 GM code: F90.0, F90.1 or F90.9) diagnosis before the first observed depression diagnosis
- 3. Must have been continuously insured by AOK PLUS during the entire study period

The patient specific index date was defined as the date of the first depression diagnosis. Baseline characteristics such as age, sex, CCI and mental health comorbidities were measured within 12 months before index. In addition, incidence rate of ADD by any physician and frequency of mental health comorbidities were observed from the patient's specific index date until the end of the follow-up period, or the patient's death. Additionally, to assess the risk factors associated with potential misdiagnosis, a multivariate cox regression analysis was conducted.

Results

STUDY POPULATION

- 196,480 patients were included in the study population based on inclusion criteria.
- Table 1 outlines the baseline characteristics of the study population measured 12 months before index for the total population and disaggregated by sex.
- There was a 37.6 percentage point difference between the percentage of females and males identified in the study population
- The average age of the patient at their first observed depression diagnoses during the study period was 58.2 years old
- More females were diagnosed with each of the top 5 mental health comorbidities compared to men
- 37.1% of outpatient diagnoses were observed by specialist in psychiatry and psychotherapy (physician code: 58) and 34.6% were observed by a phycological psychotherapist (physician code: 68)

INCIDENCE RATE OF ADD

- Out of the 196,480 patients identified depression, 858 (0.44%) patients were diagnosed with ADD and identified to have a potential misdiagnosis
- Of the 858 patients, 78.32% received a confirmed ADD diagnoses in contrast to a suspected diagnosis
- The incident rate was 0.65% (N=397) in males and 0.35% (N=461) in females (Figure 1).
- Mental health comorbidities observed within those with ADD in the follow up were anxiety and depressive disorder (12.70%), anxiety disorder (10.2%), panic disorder (9.56%), generalized anxiety (7.58%), and dysthymic disorder (6.41%)

The average age of patients with newly diagnosed ADD was 36.9 years old (males: 35.7 years, females: 38.0 years)

Table 1: Baseline Characteristics of Study Population

	Total	Male	Female
	(N=196,480)	(N= 61,340)	(N=135,140)
Sex (N,%)			
Male	61,340 (31.2%)	_	-
Female	135,140 (68.8%)	_	-
Setting of index depression diagnosis (N,%)			
Inpatient	88,978 (45.3%)	29,511 (48.1%)	59,467 (44.0%)
Outpatient	107,502 (54.7%)	31.829 (51.9%)	75,673 (56.0%)
Age (Mean, SD)	58.5 (20.2)	56.7 (19.0)	59.3 (20.7)
CCI* (Mean, SD)	2.34 (2.89)	2.57 (3.16)	2.24 (2.76)
Top 5 mental health comorbidities (N,%)			
Anxiety and Depressive disorder (ICD-10 GM** F41.2)	21,834 (11.1%)	5,373 (8.8%)	16,461 (12.2%)
Anxiety Disorder (ICD-10 GM F41.9)	16,900 (8.6%)	4,180 (6.8%)	12,720 (9.4%)
Panic Disorder (ICD- 10 GM F41.0)	15,706 (8.0%)	4,325 (7.1%)	11,381 (8.4%)
Generalized Anxiety Disorder (ICD-10 GM F41.1)	12,963 (6.6%)	3,182 (5.2%)	9,781 (7.2%)
Insomnia and Sleep Disorder (ICD-10 GM G47.0)	11,047 (5.6%)	3,303 (5.4%)	7,744 (5.7%)

*Charlson Comorbidity Index **International Classification of Diseases - German modification

Limitations

The AOK PLUS database contains data from routine practice, thus may exhibit missing data and coding errors regarding outpatient diagnoses. However, the coding of German claims data is generally considered to be of high quality.

The potential for misclassification of disease status, exists because patients are identified through diagnosis instead of medical records and, therefore, are subject to data coding limitations and data entry errors.

Additionally, there is no exact measure of misdiagnosis within the dataset, therefore, a proxy was used to estimate the potential misdiagnosis.

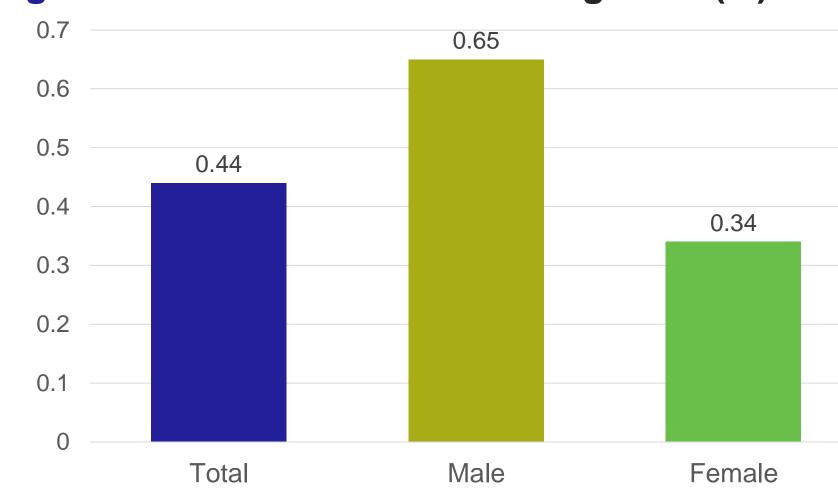
Conclusions

Despite the literature that states that females are more likely to be misdiagnosed with depression, males are more likely to be diagnosed with ADD after an initial depression diagnosis.

Even though, females are diagnosed with depression at a higher rate than males and have more comorbidities linked to ADD. Males have a higher incidence rate of ADD diagnosis after initial depression diagnosis and the Cox-regression supported this finding as well.

Further research should be conducted to measure the sexual bias of existing ADD diagnostic tools.

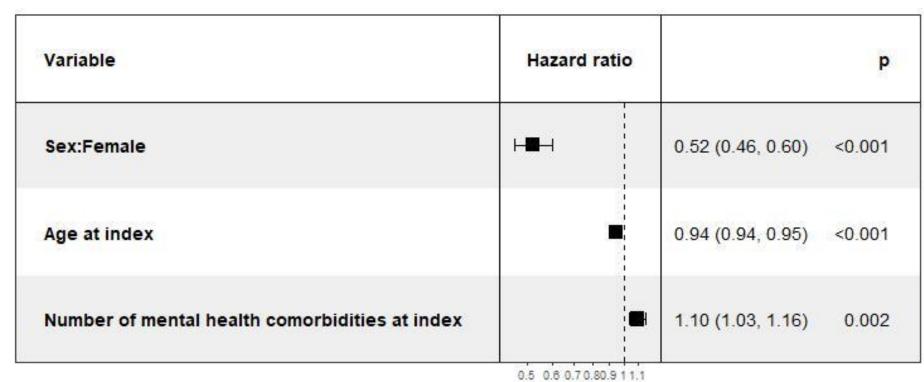
Figure 1: Incident rate of ADD diagnosis (%)



FACTORS ASSOCIATED WITH POTENTIAL MISDIAGNOSIS

- Based on the Kaplan Meier estimation, the restricted mean time to the ADD diagnosis after the initial depression diagnosis was 5.48 years.
- The Cox-regression analysis indicated that males (Hazard Ratio (HR): 0.52, p<0.001), younger patients (HR: 0.94, p<0.001) and those with more mental health comorbidities (HR: 1.10, p=0,002) were more likely to receive an ADD diagnosis after being initially diagnosed with depression (Figure 2).

Figure 2: Cox-regression forest plot



Mental health comorbidities was defined by a list of ICD-10 codes and encompasses but was not limited to ICD-10 GM groups and subgroups F41, F40, F31, F34, F30.9, F42, G47, G25, F50, F95,R44

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