

# Sex-specific manifestation of genetic risk for attention deficit hyperactivity disorder in the general population

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## Abstract

### Background

Attention deficit hyperactivity disorder (ADHD) is more commonly diagnosed in males than in females. A growing body of research suggests that females with ADHD might be underdiagnosed or receive alternative diagnoses, such as anxiety or depression. Other lines of reasoning suggest that females might be protected from developing ADHD, requiring a higher burden of genetic risk to manifest the disorder.

### Methods

We tested these two hypotheses, using common variant genetic data from two population-based cohorts. First, we tested whether females and males diagnosed with anxiety or depression differ in terms of their genetic risk for ADHD, assessed as polygenic risk scores (PRS). Second, we tested whether females and males with ADHD differed in ADHD genetic risk burden. We used three different diagnostic definitions: registry-based clinical diagnoses, screening-based research diagnoses and algorithm-based research diagnoses, to investigate possible referral biases.

### Results

In individuals with a registry-based clinical diagnosis of anxiety or depression, females had higher ADHD PRS than males [OR(CI) = 1.39 (1.12–1.73)] but there was no sex difference for screening-based [OR(CI) = 1.15 (0.94–1.42)] or algorithm-based [OR(CI) = 1.04 (0.89–1.21)] diagnoses. There was also no sex difference in ADHD PRS in individuals with ADHD diagnoses that were registry-based [OR(CI) = 1.04 (0.84–1.30)], screening-based [OR(CI) = 0.96 (0.85–1.08)] or algorithm-based [OR(CI) = 1.15 (0.78–1.68)].

### Conclusions

This study provides genetic evidence that ADHD risk may be more likely to manifest or be diagnosed as anxiety or depression in females than in males. Contrary to some earlier studies, the results do not support increased ADHD genetic risk in females with ADHD as compared to affected males.