

# Comprehensive disease-based phenotyping of comorbid disorders in children with ADHD

## Findings of a nationwide study in Germany

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### BACKGROUND

Children with attention-deficit/hyperactivity disorder (ADHD) have a higher risk of other psychiatric disorders suggesting a possible shared aetiology of psychiatric diseases. In particular, evidence exists for genetic overlapping with bipolar disorder, major depressive disorder and schizophrenia. In addition, a number of studies showed positive links of ADHD with various somatic diseases, such as asthma, obesity, diseases of the eye, and other diseases.

### AIM

In contrast to other studies that focussed on specific diseases or disease groups, we applied a hypothesis-free exploratory approach to examine the full spectrum of comorbid disorders in children with ADHD using the nationwide ambulatory claims data of statutory health insured (SHI) individuals covering approximately 90% of the total German population.

### RESULTS

Of children with ADHD, 221,548 (86%) had at least one comorbid disease compared with 40% in the control group (Fig. 1). Multimorbidity was also more common in children with ADHD (Fig. 1). As expected, the most common disease group in children with ADHD was mental and behavioral diseases (69%), followed by respiratory diseases (30%), diseases of the eyes (16%), metabolic and skin diseases (each 12%) (Table). Of the total 864 disorders examined, 370 (43%) were significantly associated with ADHD at the significance level of  $5.79 \times 10^{-5}$  (Fig. 2). Only one disorder ('para- and tetraplegia') was negatively associated with ADHD (OR: 0.51).

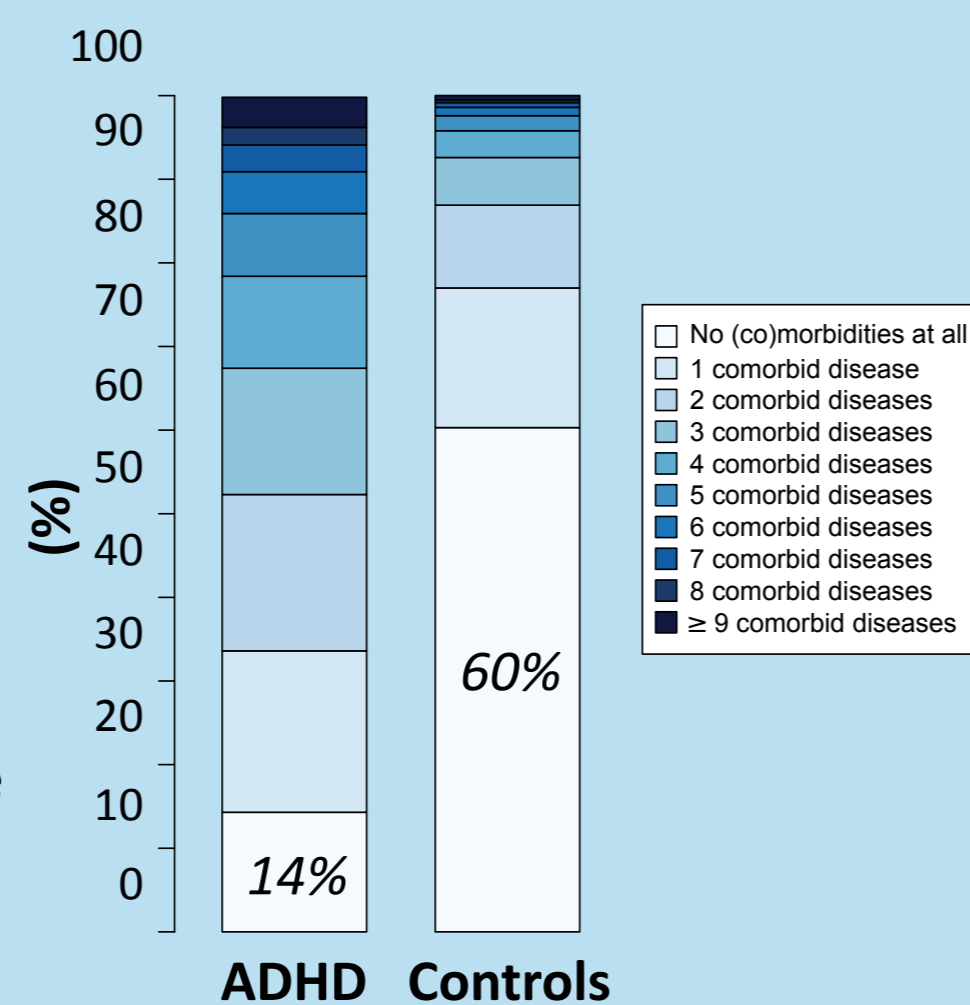


Fig. 1. Numbers of comorbidities among children with and without ADHD

Table. Prevalence of comorbidities among children with and without ADHD

Disease group	ICD-10	ADHD		Controls	
		Rank	Prevalence (%)	Rank	Prevalence (%)
mental / behavioural	F00-F99	1	69.3	2	11.0
respiratory system	J00-J99	2	29.6	1	18.2
eye / adnexa	H00-H90	3	16.0	3	8.6
metabolic	E00-E90	4	11.6	6	4.3
skin	L00-L99	5	11.5	4	6.0
infectious	A00-B99	6	8.6	5	5.4
musculoskeletal system	M00-M99	7	7.7	7	4.3
digestive system	K00-K93	8	5.3	9	2.4
nervous system	G00-G99	9	5.1	11	1.6
ear / mastoid process	H60-H95	10	4.3	8	2.4
genitourinary system	N00-N99	11	3.7	10	1.1
blood, immune	D50-D89	12	2.0	13	0.87
circulatory system	I00-I99	13	1.9	14	0.71
neoplasms	C00-C48	14	1.6	12	1.1

Positive associations were observed in all other disease groups (Fig. 3). For example, children with ADHD had higher odds of metabolic disorders (OR = 9.18), viral pneumonia (OR=4.95), disorders of white blood cells (OR=4.55), kidney failure (OR = 3.33), hypertension (OR = 3.26), obesity (OR = 2.85), type 2 diabetes (OR = 2.61), migraine (OR = 2.49), asthma (OR = 2.19), and juvenile arthritis (OR = 1.56).

### CONCLUSIONS

This study provides a comprehensive picture of comorbid disorders in children with ADHD based on a nationwide sample of children. Along with psychiatric diseases, various somatic diseases were more common in children with ADHD. The findings of this study indicate the need for a multidisciplinary approach for patient care. Physicians should be aware of a wide variety of comorbid disorders in patients with ADHD to ensure fine-grained diagnostics and adequate therapy. Early diagnostics and subsequent therapy may improve the quality of life of patients with ADHD and their family members.

### METHODS

**DATA:** Nationwide outpatient claims data of SHI-physicians  
**STUDY POPULATION:** Children and adolescents between 5 and 14 years  
**STUDY YEAR:** 2017  
**STUDY DESIGN:** A case-control study with a 1:9 case-to-control ratio  
**CASE ASCERTAINMENT:** Children with diagnoses of F90.- "hyperkinetic disorders" in at least two quarters of 2017 (n=258,662)  
**CONTROLS:** Children without any single diagnosis of F90.- since 2009 matched by gender, age and region of residence (n=2,327,958)  
**COMORBID DISORDERS:** 864 disorders from 14 disease groups at the level of the first three characters of the ICD-10 disease codes  
**ANALYSIS:** Odds ratios and 95% confidence intervals  
**STATISTICAL SIGNIFICANCE:** A Bonferroni corrected p value of  $5.79 \times 10^{-5}$  (i.e. 0.05/864)

### RESULTS

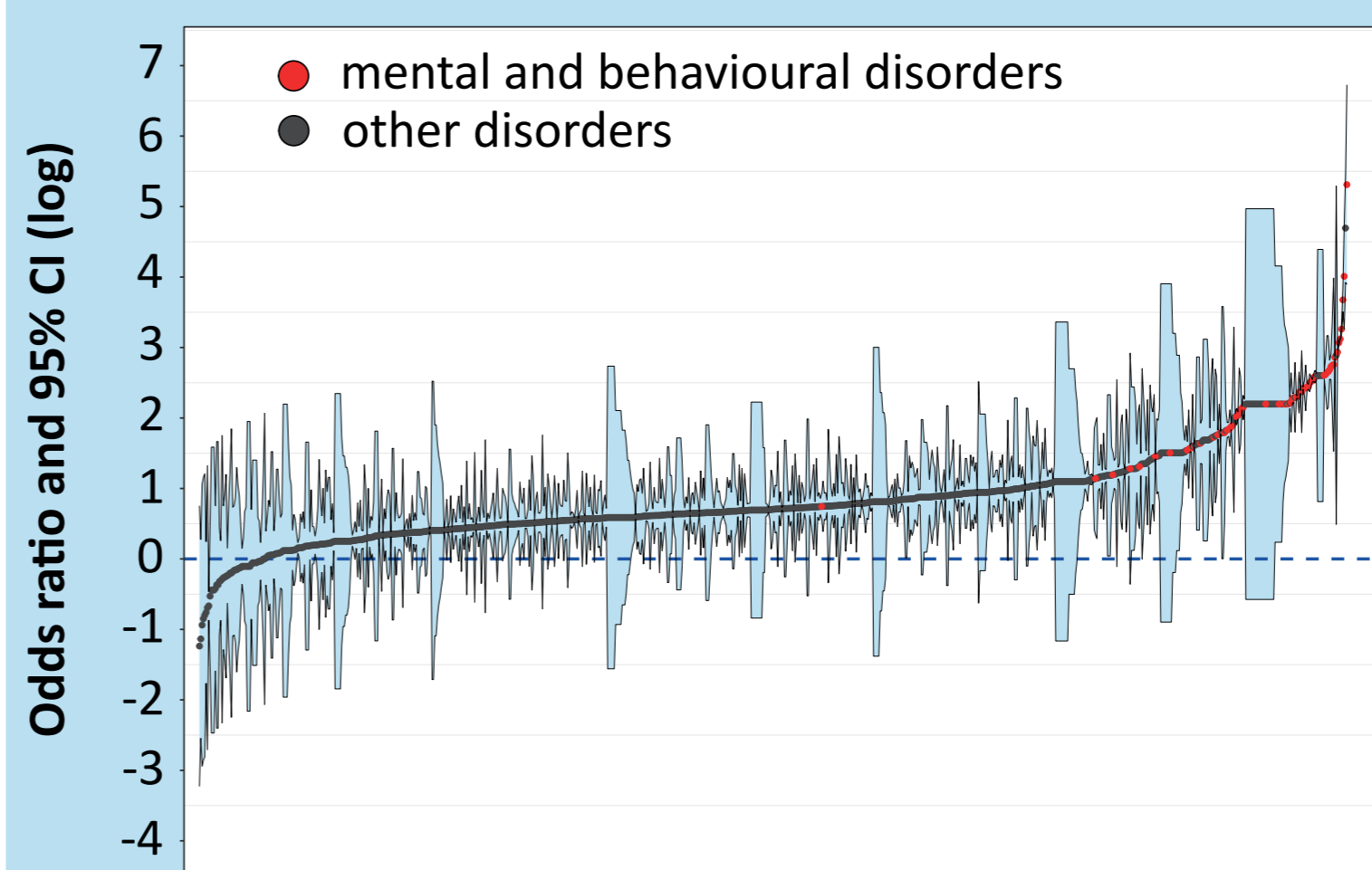


Fig. 2. Caterpillar plot of odds ratios (log) for the chance of a comorbid disease in children with ADHD

Diseases based on three characters of an ICD-10 code (n=864)

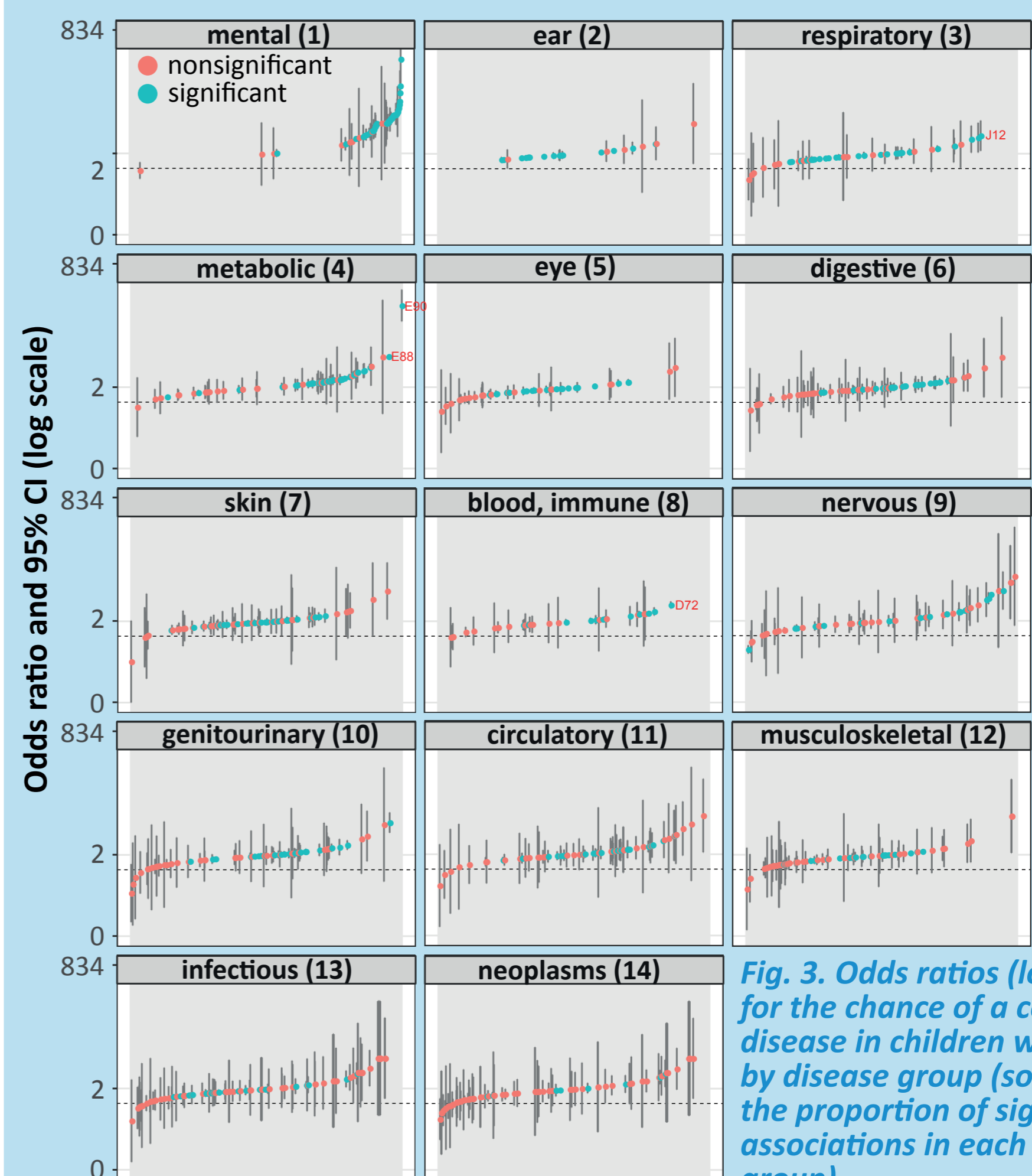


Fig. 3. Odds ratios (log scale) for the chance of a comorbid disease in children with ADHD, by disease group (sorted by the proportion of significant associations in each disease group)

Diseases based on three characters of an ICD-10 code