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Influence of gender on Attention-Deficit/ Hyperactivity Disorder in Europe – ADORE

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■ **Abstract** *Background* Attention-deficit/hyperactivity disorder (ADHD) in girls in Europe is poorly understood; it is not known whether they exhibit similar symptom patterns or co-existing problems and receive the same type of treatment as boys. *Objective* To examine gender differences for referral patterns, social demographic factors, ADHD core symptomatology, co-existing health problems, psychosocial functioning and treatment. *Methods* Baseline data from the ADHD Observational Research in Europe (ADORE) study, a 24-month, naturalistic, longitudinal observational study in 10 European countries of children (aged 6–18 years) with hyperactive/inattentive/impulsive symptoms but no

previous diagnosis of ADHD, were analysed by gender. *Results* Data from 1,478 children were analysed: 231 girls (15.7%) and 1,222 boys (84.3%) (gender data missing for 25 patients). Gender ratios (girl:boy) varied by country, ranging from 1:3 to 1:16. Comparisons showed few gender effects in core ADHD symptomatology and clinical correlates of ADHD. Compared with boys, girls had significantly more parent-rated emotional symptoms and prosocial behaviour and were more likely to be the victim of bullying and less likely to be the bully. Girls and boys had similar levels of co-existing psychiatric and physical health problems, and received the same type of treatment. *Conclusions* Fewer girls than boys are referred for ADHD treatment, but they have a similar pattern of impairment and receive similar treatment.

■ **Key words** ADHD – girls – gender differences – Europe

Abbreviations

| | | | |
|------------|---|---------|--|
| ADHD | Attention-Deficit/Hyperactivity Disorder | CHIP-CE | Child Health and Illness Profile – Child Edition |
| ADORE | Attention-deficit/hyperactivity Disorder Observational Research in Europe | CGAS | Children's Global Assessment Scale |
| ADHD-RS-IV | ADHD Rating Scale-IV | CGI-S | Clinical Global Impression – Severity scale |
| CD | Conduct Disorder | HRQoL | Health-Related Quality of Life |
| | | MTA | Multimodal treatment study of children with ADHD |
| | | ODD | Oppositional Defiant Disorder |

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a commonly diagnosed psychiatric condition in childhood. It has an estimated prevalence among school-aged children and adolescents in the United States (US), Canada, Australia and Europe of 2–18%, depending on the diagnostic criteria used [7, 10, 16, 24, 30, 33]. ADHD is less common in girls than boys [3]. Using the DSM-IV criteria, the British Child and Adolescent Mental Health Survey 1999 found a population prevalence of 2.2% of any ADHD, and a 1:4 ratio in girls compared to boys [11]. However, the gender ratio varied for the different subtypes of ADHD: 1:5 for the combined type, 1:3 for the inattentive type and 1:7 for the hyperactive-impulsive type. A systematic review of ADHD in the US school-aged population found a gender ratio of 1:3 [17].

In the clinical setting, subjects with ADHD are predominantly male, with reported gender ratios of up to 1:9 [12, 32]. As a result, there is little information about the manifestations of ADHD in girls and any differences between the genders. A 1997 meta-analysis of gender differences in ADHD suggested that phenotypic expression of the disorder resulted in referral of more boys than girls [12]. The under-referral of girls with ADHD has potentially serious public health consequences since long-term problems related to the disorder include social, academic and emotional difficulties [29].

Most of what is known about the relative characteristics of boys and girls with ADHD comes from clinic-based studies comparing boys and girls with ADHD or comparing girls with and without ADHD [6, 12, 13, 19]. The findings relating to gender differences are variable, probably due to differences in sample characteristics and in the criteria used to define the disorder. Some studies report few differences in symptomatology and co-existing problems between the genders, with the exception of less disruptive behaviour in girls [6, 32], while others suggest that adolescent girls may suffer more anxiety, depression and peer rejection than boys [26] or younger girls with ADHD [19]. A historical follow-up of clinically-referred girls with ADHD showed that they were 2.4 times more likely than boys to have a psychiatric admission in adulthood [8].

While gender differences may be an artefact of clinical referral rather than a reflection of inherent characteristics of the disorder, they have been reported between clinical and community populations. The meta-analysis of Gaub & Carlson [12] indicated no differences between girls and boys in impulsiveness, social and peer functioning and academic performance, although girls rated lower on hyperactivity and external-

ising problems. Findings from the Multimodal Treatment Study of Children with ADHD (MTA) in the US showed that girls with ADHD were generally less symptomatic than boys, especially in their levels of impulsivity [20]. In particular, girls with co-existing anxiety problems had lower levels of ADHD symptoms [20]. Consistent with the findings of Gaub and Carlson [12], girls with ADHD from the MTA study engaged in less externalising behaviour and rule-breaking [20]. These findings are in agreement with those from a large number of boys and girls with ADHD ascertained from paediatric and psychiatric referrals at a clinical and research program in paediatric psychopharmacology [6].

Although concerns have been raised about a possible referral bias in girls, few studies have evaluated gender effects in non-referred subjects. Gender differences in children meeting the symptom criteria for ADHD were recently studied in a nationally representative sample of Australian children [15]. When all ADHD types were considered together, boys and girls did not differ on core symptoms, co-morbidity or impairment, with the exception that girls rated higher on somatic complaints and boys showed poorer school functioning. However, gender patterns varied across ADHD types, with girls showing less impairment than boys in the combined and hyperactive-impulsive groups, but equal or more impairment in the inattentive group [15]. A recent study of non-referred subjects with ADHD suggested that males and females did not differ in DSM-IV subtypes of ADHD, psychiatric co-morbidity or treatment history, and showed similar levels of psychosocial, school and family functioning [5].

There are strong arguments for early intervention for affected children of both genders to reduce the likelihood of a poor long-term prognosis [29]. Although recognised in university clinics and clinical studies in European countries, it remains unclear whether girls with ADHD are recognised in diverse clinical settings across Europe and receive the same type of treatment as boys. It has been argued that because females tend to have inattentive symptoms that are less easily recognised than other symptoms, they may have to wait longer than boys for assessment and treatment. Evidence from the US indicates that during the 1990s, there was an increase in the psychopharmacological treatment of girls, younger children and children with inattentive problems [27]. However, it is not known whether the same trend is seen across the health care systems in European countries.

The present study used data collected across different regions of Europe to examine ADHD gender patterns for referral, social demographic factors, ADHD symptomatology and associated impairment, co-existing psychiatric disorders, health problems and treatment. Based on the available literature, we hypothesised that girls referred to clinics across Europe would show similar lev-

els of the core symptoms of ADHD, be equally impaired as a result of the disorder and show less externalising problems and more internalising problems than boys at the time of referral.

Methods

■ Protocol and instruments

ADORE is a longitudinal, observational, naturalistic, multi-centre study in 10 European countries: Austria, Denmark, France, Germany, Iceland, Italy, the Netherlands, Norway, Switzerland and the United Kingdom (UK). In this 2-year study, the diagnosis, treatment patterns and outcome of treatment in patients with hyperactive/impulsive/inattentive symptoms not previously diagnosed with ADHD, are being studied.

Data are collected via a core data collection form administered by the physician responsible for the assessment and treatment of the child, typically a paediatrician or a child and adolescent psychiatrist in a public or private setting. Children enrolled in the study were aged 6–18 years, with hyperactive/inattentive/impulsive symptoms, but no previous diagnosis of ADHD or a hyperactive/inattentive/impulsive syndrome in the past.

Symptoms of ADHD and the severity of disorder were assessed by the investigator using the ADHD-Rating Scale-IV-Parent version (ADHD-RS-IV) [9], the Children's Global Assessment Scale (CGAS) [31] and the Clinical Global Impression-ADHD severity scale (CGI-S) [18]. In addition, somatic and psychiatric problems, variables related to psychosocial functioning and the treatment itself, were assessed by the investigator.

To obtain information about associated behavioural and emotional problems and prosocial behaviour, the widely used 25-item Strength and Difficulties Questionnaire (SDQ) [14, 25] was completed by the parents. In addition, the parents completed the Child Health and Illness Profile-Child Edition (CHIP-CE) [23]. The CHIP-CE measures overall health-related quality of life (HRQoL) and provides information about patient mental health, self-esteem, general behaviour and involvement with family and peers.

The primary objectives of the study, the study design and data collection procedures have been described in detail elsewhere [21, 22].

■ Analyses

The ADHD-RS-IV scores were used to retrospectively classify children according to their DSM-IV ADHD subtype as follows: for children with CGAS scores ≤ 60 , the inattentive ADHD subtype was defined as having six or more inattentiveness items rated as 'often' or 'very often',

the hyperactive-impulsive ADHD subtype was defined as having six or more hyperactivity-impulsivity items rated as 'often' or 'very often', and the combined inattentive and hyperactive-impulsive ADHD subtype was defined as having six or more inattentiveness items rated as 'often' or 'very often' and six or more hyperactivity-impulsivity items rated as 'often' or 'very often'. Children with CGAS scores > 60 and/or fewer than six inattentiveness items or six hyperactivity-impulsivity items rated 'often' or 'very often' were classified as having no ADHD.

Co-existing anxiety, depression, conduct disorder (CD) and oppositional defiant disorder (ODD) were considered significant if the patient was rated as 'moderately', 'markedly', 'severely' or 'very severely ill' as a result of that problem. The proportion of patients with other psychiatric disorders and physical health problems, including asthma and epilepsy, was assessed if it was judged to be present and significantly interfering with the child's health.

The association between gender and categorical variables was analysed using a Cochran-Maentel-Haenzel test. ANOVA was used for continuous variables. In the analysis of gender-related differences, we controlled for age and disease severity (CGI-S) to take account of any differences due to these variables. All analyses were performed using the SAS statistical package and statistical testing was performed at a 5% significance level.

Results

■ Social demographic characteristics

A total of 1,573 children and adolescents from 10 European countries were enrolled in the study, but 95 patients were excluded from the analysis, giving 1,478 patients available for analysis at baseline. Of these patients, 231 (15.7%) were girls and 1,222 (84.3%) were boys (a ratio of 1:5); gender data were missing for 25 patients. The baseline social demographic characteristics of the total study population and by gender are presented in Table 1. The sample of girls was somewhat younger, with a mean age of 8.8 (SD 2.3) years compared with 9.0 (SD 2.5) years for boys (not significant). Otherwise, girls and boys were similar in social demographic characteristics. A positive family history of ADHD was somewhat more frequent in girls than boys (70.2% and 62.4%, respectively, $p = 0.017$).

As shown in Table 2, the sample of girls came predominantly from Germany (39.8%), with France, the Netherlands and the UK each providing approximately 13% of girls; each of the other six countries provided only a small number of girls. The gender distribution of patients in each country was highly variable, ranging from 1:3 in Norway to 1:16 in Austria (Table 2).

Table 1 Social demographic variables by gender

| Variable | Girls | Boys | Total sample | Test statistic*, df | P-value* |
|--|------------|------------|--------------|---------------------|----------|
| Mean (SD) age at baseline, years | 8.8 (2.3) | 9.0 (2.5) | 9.0 (2.5) | | NS |
| Age groups | | | | | |
| < 11 years | 191 (83.8) | 903 (75.7) | 1110 (76.9) | | NS |
| ≥ 11 years | 37 (16.2) | 290 (24.3) | 334 (23.1) | | NS |
| Employed parents ^a | | | | | |
| Mothers in paid employment | 128 (66.0) | 640 (65.6) | 786 (65.8) | | NS |
| Unskilled manual and clerical | 56 (28.9) | 243 (24.9) | 304 (25.5) | | NS |
| Skilled manual and sales and supervisory | 45 (23.2) | 275 (28.2) | 328 (27.5) | | NS |
| Managerial and professional | 24 (12.4) | 109 (11.2) | 138 (11.6) | | NS |
| Unspecified | 3 (1.5) | 13 (1.3) | 16 (1.3) | | NS |
| Not in paid employment | 66 (34.0) | 336 (34.4) | 408 (34.2) | | NS |
| Fathers in paid employment | 157 (94.0) | 827 (92.6) | 1006 (92.8) | | NS |
| Unskilled manual and clerical | 33 (19.8) | 145 (16.2) | 182 (16.8) | | NS |
| Skilled manual and sales and supervisory | 88 (52.7) | 473 (53.0) | 573 (52.9) | | NS |
| Managerial and professional | 31 (18.6) | 183 (20.5) | 220 (20.3) | | NS |
| Unspecified | 5 (3.0) | 26 (2.9) | 31 (2.9) | | NS |
| Not in paid employment | 10 (6.0) | 66 (7.4) | 78 (7.2) | | NS |
| Family history of ADHD | 139 (70.2) | 632 (62.4) | 785 (63.6) | 5.674, 1 | 0.017 |

Data are expressed as number (%) unless indicated otherwise

^a Excluding French patients

* Categorical variables from Cochran-Mantel-Haenszel test (Chi-square test) adjusting for age, CGI-S and gender. Age: ANOVA (F-test) adjusting for CGI and gender

The data for the girls and boys columns together does not equal the total sample due to missing gender data for 25 patients

Table 2 Gender distribution by country

| Country | Girls | Boys | Total | Gender ratio |
|----------------|------------|-------------|--------------|--------------|
| Austria | 4 (1.7) | 66 (5.4) | 73 (4.9) | 1:16 |
| Denmark | 3 (1.3) | 29 (2.4) | 32 (2.2) | 1:10 |
| France | 30 (13.0) | 211 (17.3) | 241 (16.3) | 1:7 |
| Germany | 92 (39.8) | 342 (28.0) | 434 (29.4) | 1:4 |
| Iceland | 10 (4.3) | 37 (3.0) | 47 (3.2) | 1:4 |
| Italy | 14 (6.1) | 88 (7.2) | 109 (7.4) | 1:6 |
| Netherlands | 29 (12.6) | 174 (14.2) | 212 (14.3) | 1:6 |
| Norway | 13 (5.6) | 37 (3.0) | 50 (3.4) | 1:3 |
| Switzerland | 6 (2.6) | 49 (4.0) | 57 (3.9) | 1:8 |
| United Kingdom | 30 (13.0) | 189 (15.5) | 223 (15.1) | 1:6 |
| Overall | 231 (15.7) | 1222 (84.3) | 1478 (100.0) | 1:5 |

Data are presented as number (%) patients

The data for the girls and boys columns together does not equal the total sample due to missing gender data for 25 patients

■ Symptom severity

ADHD-RS-IV scores were generally high for both genders and there were no significant gender differences in mean ADHD-RS-IV scores (Table 3). The ADHD subtypes based on scale scores were observed with similar frequency in both genders. The combined inattentive and hyperactive-impulsive subtype was the most fre-

quent ADHD subtype (39.2%), followed by the inattentive subtype (13.6%). A proportion of children (44% of girls and 41.8% of boys) were classified as not having ADHD on the basis of their ADHD-RS-IV and CGAS scores.

There were no gender differences in the parent-rated SDQ total scores (Table 3, see also Becker et al. [4]). However, girls had significantly more SDQ emotional symptoms and more prosocial behaviour than boys. Mean scores for SDQ conduct problems and hyperactivity-inattention were also lower for girls compared with boys. The broad range of behavioural and emotional problems in our sample is reflected by the high mean scores on all scales of the parent-rated SDQ. These scores can be compared to the mean parent SDQ scores for the general British population aged 5–15 years [available at www.sdqinfo.com]: total difficulties 8.4 (girls 7.8, boys 9.1); hyperactivity-inattention 3.5 (girls 2.9, boys 4.0); emotional symptoms 1.9 (girls 2.0, boys 1.8); conduct problems 1.6 (girls 1.5, boys 1.7); prosocial behaviour 8.6 (girls 8.9, boys 8.4) and peer relationship problems 1.5 (girls 1.4, boys 1.5). Our results indicate that girls in the present study have more hyperactivity-inattention and emotional symptoms but less prosocial behaviour compared with girls in the general British population.

The mean (SD) scores for each of the CHIP-CE domains were below 43 for both genders, indicating poor

Table 3 Scale scores and ADHD classification by gender

| Scale | Girls | Boys | Total sample | Test statistic*, df | p-value* |
|-------------------------------------|-------------|-------------|--------------|---------------------|----------|
| ADHD-RS-IV scores | | | | | |
| Total | 35.7 (9.5) | 35.9 (9.2) | 35.8 (9.2) | 0.016, 1 | 0.898 |
| Inattention subscale | 19.2 (4.5) | 18.8 (4.7) | 18.9 (4.7) | 3.638, 1 | 0.057 |
| Hyperactivity-impulsivity subscale | 16.5 (6.8) | 17.1 (6.0) | 16.9 (6.2) | 1.793, 1 | 0.181 |
| ADHD classification, n (%) | | | | 4.102, 3 | 0.251 |
| Inattentive | 30 (16.5) | 124 (12.8) | 159 (13.6) | | |
| Hyperactive-impulsive | 8 (4.4) | 54 (5.6) | 62 (5.3) | | |
| Inattentive + hyperactive-impulsive | 64 (35.2) | 385 (39.8) | 459 (39.2) | | |
| No ADHD | 80 (44.0) | 405 (41.8) | 490 (41.9) | | |
| SDQ scores | | | | | |
| Total difficulties | 20.4 (6.1) | 20.4 (6.0) | 20.4 (6.0) | 0.012, 1 | 0.913 |
| Emotional symptoms | 4.5 (2.4) | 3.9 (2.4) | 4.0 (2.4) | 13.340, 1 | <0.001 |
| Conduct problems | 4.2 (2.3) | 4.5 (2.3) | 4.5 (2.3) | 2.852, 1 | 0.091 |
| Hyperactivity-inattention | 8.0 (2.0) | 8.3 (1.7) | 8.3 (1.7) | 5.578, 1 | 0.018 |
| Peer relationships problems | 3.7 (2.4) | 3.7 (2.5) | 3.7 (2.5) | 0.006, 1 | 0.937 |
| Prosocial behaviour | 7.3 (2.1) | 6.7 (2.3) | 6.8 (2.3) | 14.540, 1 | <0.001 |
| CHIP-CE domain T-scores | | | | | |
| Satisfaction | 31.6 (15.0) | 32.9 (14.3) | 32.8 (14.4) | 2.979, 1 | 0.085 |
| Comfort | 40.8 (10.4) | 42.7 (10.6) | 42.5 (10.6) | 6.386, 1 | 0.012 |
| Risk avoidance | 32.8 (13.5) | 29.3 (13.5) | 29.9 (13.6) | 13.550, 1 | <0.001 |
| Resilience | 36.7 (12.5) | 35.9 (12.2) | 36.0 (12.2) | 0.285, 1 | 0.593 |
| Achievement | 30.0 (10.0) | 30.4 (10.8) | 30.3 (10.6) | 0.168, 1 | 0.682 |
| CGI-S scores | | | | | |
| | 4.3 (0.9) | 4.4 (0.9) | 4.4 (0.9) | 1.370, 1 | 0.243 |
| CGI-S categories, n (%) | | | | | |
| Normal, not ill | 2 (0.9) | 5 (0.4) | 7 (0.5) | | |
| Minimally ill | 5 (2.2) | 22 (1.8) | 28 (1.9) | | |
| Mildly ill | 24 (10.5) | 116 (9.5) | 141 (9.6) | | |
| Moderately ill | 93 (40.6) | 538 (44.2) | 644 (43.8) | | |
| Markedly ill | 94 (41.0) | 448 (36.8) | 551 (37.4) | | |
| Severely ill | 11 (4.8) | 86 (7.1) | 98 (6.7) | | |
| Very severely ill | 0 (0.0) | 3 (0.2) | 3 (0.2) | | |
| CGAS score | | | | | |
| | 55.9 (11.0) | 55.1 (10.6) | 55.2 (10.6) | 0.612, 1 | 0.434 |

Data are presented as mean (SD) unless indicated otherwise

*Continuous variables (except CGI-S): ANOVA (F-test) adjusting for age, CGI-S and gender. CGI-S: ANOVA (F-test) adjusting for age and gender. Categorical variables, from Cochran-Maentel-Haenszel test (Chi-square test) adjusting for age, CGI-S and gender

The data for the girls and boys columns together does not equal the total sample due to missing gender data for 25 patients

ADHD-RS-IV ADHD rating scale-IV; CHIP-CE Child Health and Illness Profile-Child Edition; CGAS Children's Global Assessment Scale; CGI-S Clinical Global Impression-ADHD Severity; SDQ Strength and Difficulties Questionnaire

health in each of the domains (Table 3). The girls did not appear to have a better quality of life than the boys. The mean scores for the Comfort and Satisfaction domains were lower for girls compared with boys, but the girls scored significantly higher than the boys on Risk Avoidance. There was no statistically significant difference in the mean CGAS score between the genders. The majority of subjects (88%) were scored as moderately to severely ill on the CGI-S, with similar frequencies for each of the CGI-S categories for girls and boys.

■ Co-existing psychiatric, health and psychosocial problems

At least one clinician-assessed co-existing psychiatric problem significantly interfering with functioning was present in 75.7% of girls and 81.1% of boys (Table 4). Girls were equally likely as boys to be significantly impaired as a result of anxiety and/or depression (17.6% vs 17.9%), somewhat less likely to be significantly impaired by CD and/or ODD (35.8% vs 42.5%), and slightly more likely to be impaired by a learning disorder (59.2% vs 55.2%), although the differences between the genders were not statistically significant. Obsessive compulsive disorder and bipolar disorder were present in 2.1% and 0.6% of the total sample, respectively. Sleep

Table 4 Co-existing psychiatric and health problems and psychosocial features according to gender

| | Girls | Boys | Total sample | Test statistic*, df | p-value* |
|--|------------|------------|--------------|---------------------|----------|
| Co-existing psychiatric and health problems | | | | | |
| Co-morbidities (excluding somatic problems) | | | | 2.767, 2 | 0.251 |
| No co-morbidity | 56 (24.2) | 230 (18.9) | 291 (19.8) | | |
| 1 co-morbidity | 59 (25.5) | 361 (29.7) | 433 (29.4) | | |
| > 1 co-morbidity | 116 (50.2) | 626 (51.4) | 749 (50.8) | | |
| Anxiety and/or Depression | 39 (17.6) | 213 (17.9) | 255 (17.7) | 0.021, 1 | 0.885 |
| CD and/or ODD | 81 (35.8) | 512 (42.5) | 602 (41.3) | 2.522, 1 | 0.112 |
| Tics and/or Tourette's syndrome | 13 (5.7) | 108 (9.0) | 122 (8.4) | 1.784, 1 | 0.182 |
| Co-ordination problems | 68 (30.5) | 393 (33.6) | 466 (32.9) | 1.040, 1 | 0.308 |
| Learning disorders | 126 (59.2) | 624 (55.2) | 762 (55.7) | 2.464, 1 | 0.116 |
| Sleep problems | 32 (14.2) | 175 (14.5) | 208 (14.3) | 0.123, 1 | 0.726 |
| Decreased appetite | 5 (2.2) | 9 (0.7) | 14 (1.0) | 3.561, 1 | 0.059 |
| Headaches | 10 (4.4) | 68 (5.6) | 78 (5.3) | 0.216, 1 | 0.642 |
| Abdominal pain | 13 (5.7) | 39 (3.2) | 54 (3.7) | 3.755, 1 | 0.053 |
| Psychosocial features | | | | | |
| Involvement in bullying | | | | 18.300, 3 | < 0.001 |
| Victim only | 43 (19.4) | 171 (14.7) | 216 (15.4) | | |
| Bully only | 19 (8.6) | 177 (15.2) | 199 (14.2) | | |
| Victim and bully | 9 (4.1) | 109 (9.4) | 121 (8.6) | | |
| Truant from school at least once | 9 (4.1) | 58 (5.1) | 67 (4.9) | 0.005, 1 | 0.945 |
| Visit to physician for physical or behavioural problem | 57 (24.6) | 272 (22.4) | 333 (22.7) | 0.607, 1 | 0.436 |
| Visit to accident and emergency facilities | 14 (6.1) | 94 (7.7) | 109 (7.4) | 0.248, 1 | 0.618 |
| Contact with police and/or social services | 12 (5.3) | 106 (8.7) | 118 (8.1) | 1.437, 1 | 0.231 |
| Mean (SD) no. of social activities | 7.2 (10.6) | 5.6 (8.0) | 5.9 (8.5) | 7.556, 1 | 0.006 |
| Mean (SD) total score for family burden | 9.9 (5.2) | 10.5 (5.4) | 10.4 (5.4) | 1.915, 1 | 0.167 |

Data are presented as number (%) unless otherwise indicated

* Continuous variables: ANOVA (F-test) adjusting for age, CGI-S and gender. Categorical variables: Cochran-Maentel-Haenszel test (Chi-square test) adjusting for age, CGI-S and gender

For problem not present or present but does not significantly interfere with functioning of the child versus present and significantly interferes with functioning

The data for the girls and boys columns together does not equal the total sample due to missing gender data for 25 patients

CD conduct disorder; ODD oppositional defiant disorder

Note: Obsessive Compulsive Disorder was present in five girls and 25 boys (2.1% of the sample), bipolar disorder in two girls and seven boys (0.6% of the sample), and psychosis in one girl and one boy (0.1% of the sample). Asthma was present in 7% of the girls and 7.9% of the boys, epilepsy in 0.4% of the girls and 0.5% of the boys

problems were present in 40.2% of patients, but only significantly interfering for 14.2% of girls and 14.5% of boys. While decreased appetite, headaches and abdominal pain were present in 13.7%, 26.2% and 22.4% of patients, respectively, significant impairment as a result of these symptoms were noted less frequently, as shown in Table 4.

Involvement in bullying varied significantly between girls and boys as shown in Table 4. A large proportion of children (32.1% girls, 39.3% boys) were involved in bullying. Girls were more likely than boys to be involved as the victim only, and less likely to be involved as the bully only or as both the victim and bully. Girls had a significantly higher mean number of invites to social activities compared with boys (7.2 vs 5.6, respectively; $p = 0.006$). The gender differences in other psychosocial variables were small and there was no indication of a significant gender difference in rule-breaking behaviour.

■ Resource utilisation and treatment patterns

The time gap from symptom awareness to seeking and receiving treatment is summarised in Table 5 and shows similar findings for girls and boys. The mean age of children at first awareness of symptoms was 5.1 (SD 2.7) years, although parents had noted ADHD symptoms before the age of five years in 58.7% of the sample, equally frequently in boys (59.4%) and girls (55.8%). Age at first seeking treatment was between 6 and 10 years for the majority of children (72.6% girls, 64% boys), and the mean age at first seeking treatment was 7.3 (SD 2.8) years. The mean time between first awareness of a problem and seeking treatment was 2.4 (SD 2.5) years, but the duration between first awareness of symptoms and seeking treatment was longer than four years for 25% of the sample. The mean time difference between seeking treatment and diagnosis (baseline) was comparable between genders: 1.5 (SD 2.1) years for girls and 1.7 (SD 2.2) years for boys (Table 5).

Overall, girls and boys were equally likely to see a

Table 5 Time gap from symptom awareness to seeking and receiving treatment and treatment prescribed prior to and at first visit by gender

| | Girls | Boys | Total sample | Test statistic*, df | p-value* |
|--|------------|------------|--------------|---------------------|----------|
| Mean (SD) age at first awareness of symptoms, years | 5.2 (2.7) | 5.1 (2.7) | 5.1 (2.7) | 0.482, 1 | 0.488 |
| Mean (SD) age at first seeking treatment, years | 7.3 (2.5) | 7.3 (2.8) | 7.3 (2.8) | 0.440, 1 | 0.507 |
| Mean (SD) time interval between first awareness of symptoms and seeking treatment, years | 2.3 (2.5) | 2.4 (2.4) | 2.4 (2.5) | 0.039, 1 | 0.844 |
| Mean (SD) time interval between seeking treatment and ADHD diagnosis, years | 1.5 (2.1) | 1.7 (2.2) | 1.7 (2.2) | 0.510, 1 | 0.475 |
| Treatment prior to visit | | | | 6.281, 4 | 0.179 |
| No treatment | 119 (52.4) | 559 (46.6) | 692 (47.7) | | |
| Pharmacotherapy and optionally other | 4 (1.8) | 27 (2.3) | 31 (2.1) | | |
| Psychotherapy and optionally other | 42 (18.5) | 201 (16.8) | 245 (16.9) | | |
| Pharmacotherapy, psychotherapy and optionally other | 2 (0.9) | 12 (1.0) | 15 (1.0) | | |
| Other only | 60 (26.4) | 401 (33.4) | 468 (32.3) | | |
| Treatment prescribed at the first visit | | | | 4.655, 4 | 0.325 |
| No treatment | 49 (21.8) | 243 (20.6) | 294 (20.6) | | |
| Pharmacotherapy and optionally other | 66 (29.3) | 291 (24.7) | 360 (25.2) | | |
| Psychotherapy and optionally other | 38 (16.9) | 228 (19.3) | 270 (18.9) | | |
| Pharmacotherapy, psychotherapy and optionally other | 54 (24.4) | 290 (24.6) | 356 (24.9) | | |
| Other only | 18 (8.0) | 127 (10.8) | 148 (10.4) | | |

Data are presented as number (%) unless otherwise indicated

*Continuous variables: ANOVA (F-test) adjusting for age, CGI-5 and gender. Categorical variables: Cochran-Maentel-Haenszel test (Chi-square test) adjusting for age, CGI-5 and gender

The data for the girls and boys columns together does not equal the total sample due to missing gender data for 25 patients

paediatrician or a psychiatrist for assessment and treatment: 33.8% of the girls and 36.3% of the boys were seen by a psychiatrist, and 38.1% of the girls and 35.4% of the boys were seen by a paediatrician. No information on the type of investigator seen was available for 27.4% of patients. The type of investigator seen by children varied between countries (note: this most likely reflects the different types of physicians who diagnose and treat ADHD in each participating country). Paediatricians were the investigator seen most often in the Netherlands (55.2% girls, 59.8% boys) and in the UK (83.3% girls, 68.8% boys), whereas in Austria about equal proportions of children were enrolled by paediatricians (50% girls, 48.5% boys) and psychiatrists (50% girls, 51.5% boys). In the other countries, psychiatrists outnumbered paediatricians in patient enrolment, although investigator information was not available for Denmark, Iceland and Italy. The type of investigator practice was similar for girls and boys, with 57% of the children being seen in publicly funded practices and the rest being seen in private (19.1%) or a combination of private and publicly funded practice (23.9%).

There were no significant gender differences in prior treatment or in treatment prescribed at the first visit to the physician (Table 5). A small proportion of children had pharmacotherapy prior to the first study visit, which was related to co-existing problems and not to ADHD.

Discussion

This study systematically evaluated gender differences in a large range of variables of a referred sample of 231 girls and 1,222 boys participating in a longitudinal, naturalistic study of ADHD in Europe. There were no differences between the genders in age of onset, impairment related to ADHD, duration of ADHD or core ADHD symptoms. Girls and boys also had similar levels of co-existing disorders. However, parents reported more emotional symptoms and more prosocial behaviour in girls. Girls were more socially active than boys and less likely to be involved in bullying as the bully and more likely to be involved as the victim. Girls and boys received similar types of treatment.

As expected, there were considerably more boys than girls in the study population, with a gender ratio of 5:1. Our results suggest that girls with ADHD may be under-referred in some countries and that gender specific variations may have very little influence on European paediatric practice. The varying gender ratios between countries are likely to reflect variations in the administrative prevalence of the disorder, as the epidemiologic prevalence is unlikely to vary between countries [29]. The gender ratios in the German, Icelandic and Norwegian samples were closest to the ratios found in recent epidemiological studies and show that girls with ADHD are increasingly recognised and treated in some areas of Europe. For example, Norwegian register data showed a 1:5 gender ratio for ADHD diagnosis in children re-

ferred to specialist services [1]. Referral is usually based on the recognition of ADHD symptoms by parents, teachers, school psychologists and general practitioners and the availability of services [1, 29, 36].

The similar levels of ADHD core symptoms and associated impairment between genders is in agreement with the findings of a recent study of non-referred subjects [5] and a community study [15]. In contrast, however, girls in the MTA study were generally less symptomatic than boys [20]. The high SDQ scores for girls in the present sample indicate greater emotional and behavioural disturbances relative to girls in the general population. Furthermore, in agreement with previous findings in some referred samples, girls were rated somewhat higher by parents on emotional problems [26], thus partly confirming our hypothesis.

Our findings highlight the high prevalence of co-existing psychiatric problems in both genders, and the high levels of co-ordination problems, learning disorders and sleep problems. Somatic complaints such as headaches, abdominal pain and decreased appetite were no more frequent in our sample at the first visit than in general population studies [28].

A previous study has shown that girls with ADHD had higher rates of overt and relational aggression than girls without ADHD, and that these behaviours incur social costs, especially for those with the ADHD combined type [35]. In our study, the high level of these problems was evident by the high frequency of involvement in bullying as the victim, the bully or the bully and victim. Girls with ADHD were less frequently involved in bullying as the bully and more frequently involved as the victim, compared with boys with ADHD. A recent study suggested that all three types of bullying are related to gender, aggressiveness, isolation and dislikeability of the child [34].

Although a substantial proportion of both gender groups fulfilled the criteria for ADHD or hyperkinetic disorder, no more than 60% of the subjects could be assigned to an ADHD subtype on the basis of the ADHD-RS-IV scores and CGAS scores. Researchers have found that significantly impaired symptomatic youths may not always meet the categorical criteria for diagnosis, but that they will often seek treatment and should be regarded as suffering from a disorder [2]. Another explanation for this finding might be that scores on the ADHD-RS-IV were somewhat underestimated in the ADORE sample due to variations in physician familiarity and training with the scale, thus lowering the number of children who would meet the subtype criteria. Further, it is not known to what degree the investigators relied on information from teachers in their judgement of the ADHD symptoms. Without information from teachers, the symptoms of inattention, hyperactivity and impulsivity may be judged less problematic and impairing [11]. In agreement with the literature [5, 15], the

combined inattentive and hyperactive-impulsive subtype of ADHD was the most prevalent subtype in both genders, followed by the inattentive subtype.

Although it has sometimes been argued that it may be more difficult to recognise ADHD symptoms in girls than boys, the girls in the present sample did not wait longer for referral and assessment than boys. Of note, the sample of girls was slightly younger and there were no significant differences in duration from symptom awareness to treatment onset between the genders. A pattern of ADHD symptomatology in girls with a high degree of hyperactive and impulsive symptoms and behaviour problems could increase the likelihood of referral by deviating clearly from the normal behaviour patterns in girls. The long duration between symptom awareness and referral for many children demonstrates the need for interventions to educate parents, school personnel and general practitioners about the nature of ADHD [36]. However, efforts to improve the detection of psychopathology and reduce time gaps to referral are of little use unless services are able to accurately diagnose and treat ADHD within a reasonable time frame. Our findings demonstrate the potential for improvement in services by reducing the time from referral to diagnosis.

No meaningful gender differences were observed in the treatment variables. The results of the present study are not consistent with the view that girls receive inadequate treatment and suggest that once identified, ADHD is treated similarly in both genders.

Some methodological strengths and limitations may influence our findings. The intention of the ADORE study is to gather information from a sample representative of newly diagnosed European ADHD patients. Since patients and investigators were not randomised and patients were free to participate in the study, the sample is not representative of all new cases with ADHD. The sample is large and consisted of referrals from a large number of clinical investigators in varying types of practices across Europe and, therefore, should represent a picture of usual clinical practice. The study, therefore, has several features that increase the external validity of the findings. Furthermore, because this study was carried out in clinically referred children and was not an epidemiological sample, it is not representative of all girls with ADHD.

Despite these considerations, our findings in a large group of referred ADHD subjects showed that girls were as impaired as boys in core symptoms and clinical correlates of ADHD. The results expand the knowledge base of gender effects in ADHD. To improve understanding of the specific needs of girls with ADHD and elucidate which factors may contribute to under-referral, future research efforts should include examination of gender differences in the different ADHD subtypes in clinical samples as well as in a wider community-based population. Based on our findings of gender similarities and

differences across a range of measures, we suggest that future studies should examine whether under-referral of girls is due to greater difficulties in recognising the core symptoms of ADHD in the context of the somewhat better social functioning and peer relationships in girls as compared with boys.

The primary goal of ADORE is to longitudinally describe how prescribed treatment may have an impact on

outcome and quality of life in children with ADHD and their families. Future analysis of the data in this naturalistic observational study will show whether there are differential effects in outcome related to gender.

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