Drug Treatment Patterns of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents in Germany: Results from a Large Population-Based Cohort Study

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Abstract

Objective: Despite a substantial increase in total methylphenidate (MPH) prescriptions in Germany over the last 20 years, and the introduction of modified release MPH (MR MPH) and atomoxetine (ATX), remarkably little is known about treatment patterns of attention-deficit/hyperactivity disorder (ADHD) in individual patients.

Methods: Usage patterns of ADHD drugs in children and adolescents in Germany were analyzed using data from one large German health insurance including >7,200,000 members. Of those, 6210 ADHD patients newly diagnosed in 2005 were followed for a maximum of 4 years. Kaplan–Meier estimates were calculated for onset and discontinuation of ADHD drug treatment. Predictors of time until drug treatment initiation were assessed by Cox regression.

Results: During follow-up, 52.0% of ADHD subjects (53.4% of boys, 47.5% of girls) received ADHD drug treatment. The majority of them (91.6%) were started on MPH, with immediate release MPH (IR MPH) being the initial treatment choice in 75.3%. In these subjects, change to drug treatment with MR MPH in the first year occurred in 48% by switch or addition. Significant predictors of drug treatment were behavioral and emotional disorders (HR = 1.13; 95% CI 1.03–1.24) and a diagnosis of ADHD with conduct disorder (HR = 1.21, 95% CI 1.12–1.32), whereas young age showed a protective effect. After 6, 12, and 24 months of treatment initiation, 22.4%, 43.4%, and 66.3% of treated girls, and 17.8%, 36.1%, and 54.1% of treated boys had discontinued ADHD treatment.

Conclusion: Drug treatment of ADHD was relatively common in Germany and more frequent in boys than in girls. IR MPH was the predominant treatment choice at treatment initiation. Approximately 20% of treated subjects discontinued drug treatment within the first 6 months, with girls stopping drug treatment earlier than boys. The reasons for early drug discontinuation need to be further explored.

Introduction

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) is a common childhood psychiatric disorder with a worldwide prevalence of >5% (Polanczyk et al. 2007). According to the German Health Interview and Examination Survey for Children and Adolescents (KiGGS) conducted between 2003 and 2006, 4.8% of children and adolescents 3–17 years of age had ever been diagnosed with ADHD in Germany (Schlack et al. 2007). Among those who were 11–17 years of age, 1 in 10 boys and 1 in 43 girls had ever had a diagnosis of ADHD (Schlack et al. 2007). An analysis of data from one regional statutory health insurance (SHI) company in Germany has shown an increase in the prevalence of ADHD by 45% from 2000 to 2007 (Schubert et al. 2010).

Treatment of ADHD is largely conducted with methylphenidate (MPH) in Germany (Schubert et al. 2010; Lindemann et al. 2012). In Germany, MPH was launched in 1954 and was put under the controlled substances legislation in 1971. During the last 20 years, total MPH prescriptions have shown a substantial increase, multiplied by a factor of 187 from 1990 to 2010 (Fig. 1). A similar increase has not been observed for atomoxetine (ATX), although it is not subject to the controlled substances legislation in Germany and is therefore easier to prescribe. ATX was introduced into the German market in March 2005. According to the guideline of the German Society of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy (DGKJP), ATX can be considered the drug of first choice, if potential substance abuse is of concern or if efficacy throughout the day is required (Döpfner and Lehmkuhl

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FIG. 1. Annual methylphenidate and atomoxetine prescriptions in Germany in million defined daily doses (DDDs) between 1990 and 2010 (Data: German Drug Prescription Reports 1991–2011). A color version of this figure is available in the online article at www.liebertpub.com/jcap.

2007). It has also been recommended by the DGKJP in the presence of comorbid anxiety disorders, when a tic disorder is present, or if it is the patient's/family's preference.

Regarding MPH, several modified release (MR) formulations are now available in Germany. CONCERTA[®], launched in January 2003, was the first MR MPH, followed by Medikinet[®] retard (launched on February 1, 2005), Equasym[®] Retard (launched on September 15, 2006), and RITALIN LA[®] (launched on December 1, 2007). These formulations overcome the need for the multiple daily doses that are necessary with immediate release (IR) formulations because of their short half-life (Takoni 2011), and are generally considered to be as effective as the IR formulations (Coghill and Seth 2006). The MR MPH formulations differ in their MPH release profiles, thereby enabling the physician to match the medication to the patient's particular requirements (Takoni 2011). Reduced compliance and an increased potential for missed doses have been discussed as potential limitations of IR MPH formulations, together with an uneven coverage through the day and stigmatization by peers when administering IR MPH at lunch time in school (Coghill and Seth 2006).

Despite the substantial number of ADHD prescriptions, only scarce data are available on drug usage patterns in individual patients in Germany. This study was conducted to evaluate drug treatment of ADHD in children and youth in Germany with respect to the time until treatment, the initial treatment choice, switches between drugs, and persistence of drug treatment.

Methods

Source of data

The study was based on data from one large German SHI company for which data was available from 2004 through 2008 at the time of the analysis. This insurance includes data from >7,200,000 insurance members from all regions in Germany. Available data contain demographic information and information on hospital discharges, physician visits, and outpatient dispensing of prescribed medications in the pharmacies. The hospital data comprise admission and discharge dates, diagnoses associated with the admission and all discharge diagnoses, and diagnostic and therapeutic procedures with their respective dates. Claims of outpatient physician visits include outpatient diagnoses and proce-

dures. As physician visits are reimbursed on a quarterly basis, diagnoses associated with a visit can only be attributed to a quarter of a year and not to an exact date. All diagnoses are coded according to the German modification of the International Classification of Diseases (ICD-10-GM). Prescription drug information is recorded for all outpatient dispensings that are reimbursable by SHIs and includes the date of prescription, the date of the dispensing, the central pharmaceutical number (CPN), and information on the prescribing physician with the physician specialty. Via linkage of the CPN to a pharmaceutical reference database, information is available on the prescribed quantity, strength, formulation, generic and trade name, the anatomical-therapeutic-chemical (ATC) code, and the defined daily dose (DDD). In preliminary analyses, the age and sex distribution, the number of hospital admissions, and the quantity of drug use of the available SHI data have been shown to be representative for the entire German population (Pigeot and Ahrens 2008; Schink and Garbe 2010a,b).

Cohort definition

A cohort of children and adolescents 3–17 years of age, with a first diagnosis of ADHD in 2005, was identified and followed until discontinuation of insurance, death, or December 31, 2008. Cohort entry was defined as the first date of diagnosis of ADHD or prescription of MPH or ATX, whichever came first. Subjects were required to be continuously insured for at least 12 months before the date of cohort entry. To be considered a new diagnosis of ADHD, subjects were required not to have been diagnosed with ADHD and not to have received a prescription for MPH or ATX in the previous 12 months. Patients with ADHD were defined as patients who had either received one inpatient or at least two outpatient ICD-10 GM diagnoses of F90.0 (disturbance of activity and attention) or F90.1 (hyperkinetic conduct disorder), or one outpatient diagnosis of F90.0 or F90.1 with a diagnosis of F90.9 (hyperkinetic disorder, unspecified) within a time interval of 365 days, or one outpatient diagnosis of F90.0 or F90.1 and at least one prescription of MPH or ATX. Psychiatric comorbidities were ascertained in the year before cohort entry.

Exposure assessment and statistical analysis

For each patient included in the study, all prescriptions of MPH (ATC code: N06BA04) or ATX (ATC code: N06BA09) were identified. Based on their central pharmaceutical numbers, MPH drug treatment was further grouped into MR MPH formulations including Ritalin LA, Equasym retard, Concerta, Medikinet retard (Banaschewski et al. 2008), and all other MPH formulations available on the German market classified as IR MPH formulations. The proportion of subjects receiving ADHD drug treatment, the choice of the first ADHD drug, and the specialty of the first treating physician were assessed. Time until treatment initiation was analyzed overall and stratified by age, sex, ADHD subtype (F90.0 or F90.9 versus F90.1), and combinations of specific comorbidities including disorders of psychological development (F80–F89), behavioral and emotional disorders (except ADHD), and not otherwise specified psychiatric disorders (F91–F99) using the Kaplan–Meier method. Differences were tested by the log-rank test. Hazard ratios (HRs) for drug treatment initiation were calculated with Cox regression analysis, considering sex, age, ADHD subtype, psychiatric comorbidities, and the specialty of the first diagnosing physician in the analysis.

In all treated children and adolescents, the time until treatment discontinuation was analyzed with the Kaplan–Meier method. A patient was considered to discontinue ADHD treatment if a new

prescription for any ADHD drug was not filled within 3 months after the theoretical end date of the previous prescription as it had been defined in previous studies (van den Ban et al. 2010; Chen et al. 2011; Stein et al. 2012). Additionally, we conducted a sensitivity analysis using a minimum gap of only 4 weeks. Continuation of treatment was defined as another dispensation of the initially prescribed ADHD drug within 3 months of the last day covered by the previous prescription. Therapy switch was defined as changing from one type of ADHD drug to another within 3 months of the last day covered by the previous prescription. An addition of ADHD drug treatment was defined as starting another type of ADHD drug while continuing the initially prescribed drug. To further assess drug usage patterns, we studied continuation, switch, addition, or discontinuation of drug use. As information on the prescribed dosage regimen was lacking in the health insurance data, we assumed a daily dose of one tablet for MR MPH or ATX and two tablets for IR MPH. Drug usage patterns were investigated in the first year after the start of drug treatment for ADHD considering both formulations of MPH and ATX. This analysis was conducted only in patients who had at least 15 months of follow-up after starting ADHD drug treatment.

This study was conducted with permission from the Federal Ministry of Health according to the Code of Social Law (SGB X). No informed consent was required, as the analysis involved only routine and pseudonymized data.

Results

The study population consisted of 6210 ADHD patients newly diagnosed in 2005, with an average follow-up time of 3.4 years per patient. Of those, 1443 (23.2%) were girls. Most patients (68.5%) were in the age range of 6–11 years, whereas 8.7% were <6 years of age (Table 1). A total of 85.0% of female patients and 77.3% of male patients had received one or more diagnoses of F90.0 or F90.9, whereas the remaining patients had received at least one diagnosis of F90.1 (Table 1). Psychiatric comorbidities were frequent, particularly disorders of psychological development in 47.0% and behavioral and emotional disorders (without F90) in 43.1% (Table 1). For most patients, the first diagnosing physician was a pediatrician (44.5%) or a child psychiatrist (30.0%) (Table 1).

Overall, 3232 children and adolescents (53.4% of the boys and 47.5% of the girls) received any ADHD drug treatment during follow-up. Initiation of treatment by pediatricians and child psychiatrists was similar in magnitude, being 39.3% and 38.0%, respectively. Of the treated subjects, 91.6% were started on MPH and 8.4% on ATX (Table 2). Overall, 21.3% of subjects (21.6% of boys, 20.1% of girls) had already received drug treatment with the initial diagnosis (Fig. 2). Boys tended to receive ADHD drug treatment somewhat earlier than girls (Fig. 2a). The proportion of boys (girls) with a first prescription of MPH or ATX within 90, 183, and 365 days after the initial diagnosis was 29.6% (27.9%), 36.6% (34.5%), and 43.0% (39.0%), respectively. The younger age groups showed longer time intervals until treatment initiation (Fig. 2b). No difference was observed for the age groups 11–14 and 15–17 years. Subjects with a diagnosis of F90.1 were treated earlier than those who received only a diagnosis of F90.0 or F90.9 (Fig. 2c). Subjects with behavioral and emotional disorders (F91–F99) were treated earlier than those with disorders of psychological development (F80–89) (Fig. 2d). For all of the results shown in Figure 2, the corresponding log-rank tests showed significant differences (p value < 0.001) between the respective strata. In the Cox regression analysis, behavioral and emotional disorders (F91–F99) were sig-

TABLE 1. CHARACTERISTICS OF STUDY POPULATION

	Males [%] (n = 4767)	Females [%] (n = 1443)	Total [%] (n = 6210)
Age at diagnosis (years)			
3–5	9.0	7.6	8.7
6–8	36.3	34.9	36.0
9–11	31.3	36.4	32.5
12–14	18.1	14.3	17.2
15–17	5.3	6.8	5.6
Mean length of follow-up (years)	3.35	3.34	3.35
ADHD subtype			
F90.0	77.3	85.0	79.1
F90.1	10.2	7.0	9.4
both F90.0 and F90.1	12.5	8.0	11.5
Mental comorbidities			
Neurotic, stress-related and somatoform disorders (F40–48)	15.3	20.2	16.5
Disorders of psychological development (F80–89)	48.0	43.8	47.0
Behavioral and emotional disorders without hyperkinetic disorders (F91–99)	43.4	42.2	43.1
Other mental and behavioral disorders without hyperkinetic disorders (other F.. without F90)	16.1	19.2	16.8
Specialty of the first diagnosing physician			
Pediatrician	44.5	44.4	44.5
Child psychiatrist	30.1	29.8	30.0
Psychotherapist	1.7	2.0	1.8
General practitioner	11.3	11.1	11.2
Ambulatory healthcare center/hospital	7.0	7.2	7.1
Other	5.4	5.5	5.4

ADHD, attention-deficit/hyperactivity disorder.

nificant predictors of drug treatment with an HR of 1.13 (95% CI 1.03–1.24) as was having a diagnosis of ADHD with conduct disorder (F90.1) within the first year of diagnosis (HR = 1.21, 95% CI 1.12–1.32), whereas young age showed a protective effect (HR = 0.39, 95% CI 0.33–0.46 for the age group 3–5, HR = 0.81, 95% CI 0.74–0.88 for the age group 6–8, both compared with the age group 9–11). Despite controlling for other covariates, males were more likely to receive drug treatment than females (HR = 1.16, 95% CI 1.06 – 1.26).

Whereas the majority (75.3%) of all treated patients was started on IR MPH, 16.2% were started on MR MPH (Table 2). Of those patients started on IR MPH who had at least 15 months of continuous follow-up, 33.3% continued treatment with IR MPH during the first year, whereas 22.4% switched to MR MPH, and 16.6% discontinued treatment in the first year (Table 3). Addition of MR MPH to IR MPH was observed in 25.6% of patients, whereas addition of ATX was rare. Switches to ATX were only infrequently observed with 1.5% of initial IR MPH users and 2.7% of MR MPH users. In subjects started on ATX, 45% continued and 25.2% discontinued ATX treatment during the first year. Switches to MPH occurred in 26.8% (Table 3). Discontinuation did not vary by the

TABLE 2. CHARACTERISTICS OF SUBGROUP RECEIVING DRUG TREATMENT DURING FOLLOW-UP

	Males [%] (n = 2546)	Females [%] (n = 686)	Overall [%] (n = 3232)
Age at drug treatment initiation (years)			
3–5	1.3	1.2	1.3
6–8	30.0	27.4	29.5
9–11	40.1	45.8	41.3
12–14	22.5	16.6	21.3
15–17	5.7	8.9	6.4
First drug treatment			
MPH	91.5	91.8	91.6
IR MPH	75.2	75.8	75.3 ^a
MR MPH	16.3	16.0	16.2 ^a
ATX	8.5	8.2	8.4
Specialty of the first treating physician			
Pediatrician	38.3	42.9	39.3
Child psychiatrist	38.2	37.5	38.0
Psychotherapist	0.4	0.3	0.4
General practitioner	6.0	5.4	5.9
Ambulatory healthcare center/ hospital	11.2	8.6	10.7
Other	5.9	5.4	5.8

^aFigures do not add up to 91.6% (and overall to 100%) because of rounding.

MPH, methylphenidate; IR MPH, immediate release methylphenidate; MR MPH, modified release methylphenidate; ATX, atomoxetine.

ADHD subtype. Across both subtypes, 6, 12, and 24 months after treatment initiation, 22.4%, 43.4%, and 66.3% of treated girls and 17.8%, 36.1%, and 54.1% of treated boys had discontinued ADHD treatment (Fig. 3). These results did not change substantially in the sensitivity analysis when the criterion for discontinuation was reduced from 3 months to only 4 weeks (results not shown).

Discussion

Drug treatment of ADHD is relatively common in Germany, and more frequent in boys than in girls. MPH was the first drug treatment choice in most subjects. This is in line with recommendations from the DGKJP and the European Society for Child and Adolescent Psychiatry (ESCAP) (Taylor et al. 2004; Döpfner and Lehmkuhl 2007). Stimulants rapidly reduce the clinical manifestations of ADHD such as restlessness, inattentiveness, and impulsiveness; they improve the quality of social interactions and decrease aggression (Taylor et al. 2004), although a recent study did not find an improvement of attention-related cognitive functions in boys with ADHD (Hellwig-Brida et al. 2011).

At the beginning of drug treatment with MPH, the majority of patients (82.3%) were started on IR MPH formulations. IR preparations are considered during initial titration to determine correct dosing levels or may be considered if more flexible dosing regimens are required. Only 17.7% of subjects started MPH treatment on the MR formulation. According to guidelines and the German Summary of Product Characteristics (SPC), MR MPH formulations may also be used at treatment initiation (Taylor et al. 2004). As an example, the German SPC of Equasym retard specifies that treatment with the extended release formulation can be initiated if the physician thinks that initial treatment with IR MPH is not feasible (Shire 2011).

Less than 10% of subjects were started on ATX. ATX is a selective norepinephrine reuptake inhibitor (Vaughan et al. 2009) and

the only nonstimulant drug treatment that is approved for ADHD in Germany. It is only recommended as a drug of first choice in selected indications, for example when substance abuse is of concern (Döpfner and Lehmkuhl 2007). ATX is usually regarded to be of lower efficacy than MPH (Vaughan et al. 2009; Wolraich et al. 2011). Consistent with this, 27% of ATX users switched to MPH during the first year after treatment initiation, whereas only 2% of MPH users switched to ATX.

Although tolerability of treatment with MPH is generally regarded as high, and severe adverse drug reactions are rare (Taylor et al. 2004; Sonuga-Barke et al. 2009), recently concerns have arisen about some rare serious side effects of MPH or other stimulants, including a small number of sudden deaths attributed to cardiovascular events (SIGN: Scottish Intercollegiate Guidelines Network 2009). Based on these rare events reported in post-marketing surveillance, the European Medicines Agency (EMA) made several recommendations and emphasized that MPH should only be used when remedial measures alone have proved insufficient (CHMP 2009). In this respect, it is of interest that 21% of ADHD subjects in our study had already received ADHD drug treatment with their first diagnosis of ADHD. EMA also recommended that drug treatment should be interrupted at least once per year (CHMP 2009). In our study, 64% of males and 57% of females received drug treatment with MPH or ATX for > 1 year. Our study is based on data from before these recommendations by EMA were published. It remains to be seen if more recent data will provide different results.

Previous studies in Germany focused on the estimation of MPH treatment prevalence (Schmidt-Troschke et al. 2004; Schubert et al. 2010) and did not assess drug treatment patterns in ADHD patients. Based on prescription data of one large SHI in Mecklenburg-Vorpommern in the former East Germany, the prevalence study by Schmidt-Troschke et al. also analyzed the specialty of the MPH prescribing physician. This study found that MPH was prescribed most frequently by general practitioners (GPs) followed by pediatricians and neurologists (including child psychiatrists). Our study pointed to different physician specialties when we analyzed who initiated ADHD drug treatment, with pediatricians being first, followed by child psychiatrists. In only 6% of ADHD patients was drug treatment started by GPs. Another German study conducted in the city of Cologne similarly found that 71% of all MPH prescriptions were made by pediatricians (Bessou et al. 2007). This study also showed that 28% of patients received only a single prescription of MPH. However, as this study assessed prescriptions only during a 6 month period, this figure will be an overestimate of drug discontinuation, particularly as 34% of patients with single prescriptions received a prescription for 100 tablets. The results of our study showed a lower discontinuation rate during the first 6 months of ~19% (males 18%, females 22%).

Compared with studies conducted in North America (Miller et al. 2004; Marcus et al. 2005; Lawson et al. 2012), we observed a rather high percentage of subjects continuing ADHD drug treatment for >6 (81%) or 12 (62%) months. Differently, in the study by Marcus et al. based on Medicaid claims data from California in the United States, a mean treatment duration of 140 days and 103 days was reported for MR MPH and IR MPH, respectively (Marcus et al. 2005). The rather high percentage of patients continuing ADHD drug treatment in our study may partly be explained by the different diagnostic criteria used in Germany (ICD-10) and North America (DSM-IV). It is well established that DSM-IV criteria identify a broader group of subjects than the criteria used in ICD-10 (Swanson et al. 1998). This is the result of the exclusion of certain

FIG. 2. Time until first prescription of methylphenidate (MPH) or atomoxetine (ATX) overall and by sex (a), by age (b), by attention-deficit/hyperactivity disorder (ADHD) subtype (c), and by specific psychiatric comorbidities (d). Corresponding log-rank test results were: (a) $\chi^2 = 13.2$, $df = 1$, p -value = 0.0003; (b) $\chi^2 = 174.7$, $df = 4$, p -value = <0.0001; (c) $\chi^2 = 39.1$, $df = 1$, p -value = <0.0001; (d) $\chi^2 = 35.1$, $df = 3$, p -value = <0.0001. A color version of this figure is available in the online article at www.liebertpub.com/jcap.

comorbidities such as depression and anxiety in subjects with ADHD according to ICD-10 but not according to DSM-IV, and the requirement of symptoms in all three domains (inattention, hyperactivity, and impulsivity) in ICD-10 but not in DSM-IV. Also, the criteria for cross-situational pervasiveness are more rigorous in ICD-10 than in DSM-IV (Swanson et al. 1998). In line with this, the BELLA study in Germany showed a prevalence of ADHD according to DSM-IV of 5%, whereas it was 1% for the prevalence of hyperkinetic disorder diagnosed according to ICD-10 (Dopfner et al. 2008). These differences in diagnostic criteria are compatible with a more severely affected patient population of ADHD subjects according to the diagnostic criteria used in ICD-10, which may in part explain the longer ADHD treatment duration in these subjects in our study.

Some strengths and limitations of our study need to be considered. This study was based on data from a large SHI in Germany providing data on drug treatment of ADHD in everyday clinical practice over 4 years. Drug prescriptions and dispensations are well

captured in these data and are probably less subject to misclassifications than are data ascertained in personal interviews, particularly if drug treatment dating farther back has to be ascertained. These data lack, however, information on the prescribed daily dose or drug holidays. Our assumption of one tablet of MR MPH or ATX per day is based on dosing recommendations in the SPC. The assumption of two tablets of IR MPH per day may lead to some misclassification, if subjects received, for example, three tablets or only one tablet per day. We also lacked information on the compliance of the subjects, that is, whether they were taking the medication as prescribed. We did not analyze other stimulants such as amphetamines, which might be used for the treatment of ADHD. Whereas these are licensed for drug treatment of ADHD in other countries, they were not available on the German market as finished products until December 2011, and were therefore only rarely used.

In summary, during an average follow-up of 3.4 and a maximum follow-up of 4 years, >50% of subjects newly diagnosed with ADHD received ADHD drug treatment in Germany. Drug

TABLE 3. CHANGES IN ADHD DRUG TREATMENT IN THE FIRST YEAR AFTER TREATMENT INITIATION^a

Treatment patterns	First ADHD drug treatment		
	IR MPH n = 2219 %	MR MPH n = 525 ^b %	ATX n = 258 ^c %
No change (continuation)	33.3	45.5	45.0
Discontinuation	16.6	14.5	25.2
Switch to			
IR MPH	na	24.2	19.0
MR MPH	22.4	na	7.8
ATX	1.5	2.7	na
Addition of			
IR MPH	na	11.8	2.3
MR MPH	25.6	na	0.8
ATX	0.6	1.5	na

^aThis table includes only patients with at least 15 months of continuous follow-up following the definition of continuous use (see Methods section). Only the first change in treatment was considered in the analyses. The proportion of patients discontinuing treatment is therefore lower than in Figure 3, as this analysis does not include patients who discontinued treatment in the first year after a previous change (switch or addition) in treatment.

^bIncludes $n=57$ patients (10.9%) who were started on MR MPH+IR MPH.

^cIncludes $n=3$ patients who were started on ATX+IR MPH and $n=1$ patient who was started on ATX+MR MPH.

ADHD, attention-deficit/hyperactivity disorder; MPH, methylphenidate; IR MPH, immediate release methylphenidate; MR MPH, modified release methylphenidate; ATX, atomoxetine.

treatment was more frequent in boys than in girls. More than 20% of subjects were already started on drugs at first diagnosis of ADHD. Mental comorbidities and higher age at diagnosis of ADHD were significant predictors of treatment initiation. MPH was the initial treatment choice in > 90% of patients. In line with treatment recommendations, IR MPH was most frequently prescribed as the first drug and was in a large proportion of patients

FIG. 3. Time until discontinuation of attention-deficit/hyperactivity disorder (ADHD) drug treatment according to sex and ADHD subtype (Log-rank test results were: $\chi^2=24.5$, $df=3$, p -value = < 0.0001). A color version of this figure is available in the online article at www.liebertpub.com/jcap.

followed by a switch to or addition of MR MPH during the first year. Discontinuation of drug treatment occurred earlier in girls than in boys.

Conclusion

Drug treatment of ADHD is relatively frequent in Germany, with > 50% of subjects receiving drug treatment within 4 years of diagnosis. Drug treatment is more frequent in subjects with emotional and behavioral disorders and those with ADHD with conduct disorder and occurs less commonly in children at younger ages. Drug treatment is most frequently initiated by pediatricians and child psychiatrists. Approximately 20% of subjects discontinue drug treatment within the first 6 months of treatment initiation. The reasons for early discontinuation need to be further explored.

Clinical Significance

This first population-based study on ADHD drug treatment patterns provides important data on real life treatment of ADHD in Germany. Drug treatment with MPH in ADHD children and adolescents is relatively common in Germany. The predominantly observed initial choice of drug treatment with IR-MPH and subsequent switch to MR-MPH is in line with treatment recommendations.

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Disclosures

Edeltraut Garbe runs a department that occasionally performs studies for pharmaceutical industries with the full freedom to publish. The companies include Mundipharma, Bayer-Schering, Stada, Sanofi-Aventis, Sanofi-Pasteur, Novartis, Celgene, and GlaxoSmithKline. She has been consultant to Bayer-Schering, Nycomed, Teva, and Novartis in the past. The present work is unrelated to the abovementioned relationships. Rafael T. Mikolajczyk received research funding from Sanofi Pasteur MSD (SPMSD) and Bayer Pharma AG, unrelated to this project. Tobias Banaschewski served in an advisory or consultancy role for Bristol Myers-Squibb, Develco Pharma, Lilly, Medice, Novartis, Shire, and Viforpharma. He received conference attendance support and conference support or received speaker's fee from Lilly, Janssen McNeil, Medice, Novartis, and Shire. He is/has been involved in clinical trials conducted by Lilly and Shire. The present work is unrelated to the abovementioned grants and relationships. The remaining authors declare no conflict of interest.

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