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Prevalence, determinants and spectrum of attention-deficit hyperactivity disorder (ADHD) medication of children and adolescents in Germany: results of the German Health Interview and Examination Survey (KiGGS)

Hildtraud Knopf,[1] Heike Hölling,[1] Michael Huss,[2] Robert Schlack[1]

ABSTRACT

Objective: To investigate the prevalence, determinants and spectrum of attention-deficit hyperactivity disorder (ADHD) medication and its associations with socioeconomic status (SES), health-related behaviour and living conditions.

Design: Observational cross-sectional study.

Setting: Germany.

Participants: Representative population-based sample of non-institutionalised youth aged between 0 and 17 years (n=17 450) and examined between 2003 and 2006.

Main outcome measure: Prevalence and spectrum of ADHD medication (Anatomical Therapeutic Chemical (ATC) code N04BA) measured by standardised computer-assisted personal interview (CAPI) on drug use.

Results: The overall prevalence of ADHD medication (stimulants including atomoxetine) was 0.9% (95% CI 0.7% to 1.1%). Boys used these drugs (1.5%, 1.2% to 1.8%) five times more than girls 0.3% (0.2% to 0.5%). The highest prevalence rates were for boys aged 6–10 years (2.3%, 1.7% to 3.1%S) and 11–13 (2.7%, 2.0% to 3.7%). Boys from families with no immigration background used ADHD medication almost 6 times as frequently as boys with an immigration background (1.7% vs 0.3%). Multivariate analysis (binary logistic regression) showed boys (OR 5.16, 95% CI 3.15 to 8.47), 11-year-olds to 13-year-olds (2.24, 1.28 to 3.49), children in large cities (2.18, 1.13 to 4.22), children with no immigration background (3.06, 1.34 to 6.99), and children with only a good (vs excellent) parent-rated health status (1.91, 1.18 to 3.08) being more likely to be using ADHD medication. A visit to the doctor in the last month or last quarter was associated with a higher probability for ADHD medication (3.18, 1.29 to 7.95 and 3.59, 1.45 to 8.90, respectively).

Conclusions: Results show prevalence rates of ADHD medication use for the German child and adolescent population that are considerably lower than published prevalence rates from the USA, but comparable with those of western European and Scandinavian countries. Lower use rates in rural versus urban regions may point to differential healthcare access. The inverse association of

ARTICLE SUMMARY

Article focus
- To report prevalence rates and determinants of attention-deficit hyperactivity disorder (ADHD) medication use in a nationally representative sample of German youth.
- To compare these prevalence rates with published data from other developed countries.
- To report indications, substance group, origin, self-rated improvement of conditions treated, tolerance, duration of use and perceived adverse drug reactions (ADRs).

Key messages
- We find lower prevalence rates for German youth as they are reported for the USA, but comparably high rates as they are reported for Western European Countries and Scandinavia.
- When diagnosed with ADHD, 6-year-old to 10-year-old boys were significantly more likely to being treated with ADHD medication than girls.
- Lower prevalence rates in rural regions and in immigrant families may point to differential thresholds to healthcare access or may reflect culturally altered attitudes towards symptoms of ADHD, respectively.

Strengths and limitations of this study
- We provide detailed information on ADHD medication use in minors in a population-based, nationally representative sample.
- We rely on self-reported information on drug use in the last 7 days.
- The cross-sectional study design does not allow for the assessment of causal relations.

ADHD medication use with immigration status suggests potentially restricted access to healthcare services for immigrants or may reflect culture-specific differences in attitudes towards symptoms of ADHD.

INTRODUCTION

Alongside psychoeducation and behavioural interventions, the treatment of ADHD (attention-deficit hyperactivity disorder) with drugs such as methylphenidate or Atomoxetine is an essential part of multimodal treatment.[1][2] In terms of its risk–benefit ratio, pharmacotherapy has been found to be effective and to have relatively few adverse drug reactions (ADRs). The risk that ADHD medication might lead to subsequent substance abuse is regarded as low—it has even been shown to have a protective effect.[3–5] As a result, prescription statistics and epidemiological studies are reporting a growing use of these drugs. The use of stimulants by children and adolescents (<19 years) in the USA, for example, increased between 1986 and 2002 from 0.6% to 2.9%.[6] Similar increases were reported in a population-based longitudinal study in Israel for the period from 1984 to 2004 (0.7% vs 2.5%).[7] According to Hugtenburg *et al*,[8] an increase in the prescription prevalence of psychotropic drugs reported in the Netherlands from 1995 to 2001 was primarily due to an increase in prescriptions of stimulants.

Prescription data from statutory health insurance (SHI) providers in Germany show a comparable trend.[9] The drug prescription report describes a more-than-five-fold increase in prescriptions from 10 million DDDs (defined daily doses) in 1999 to 53 million DDDs in 2008.[10] The national and international increase in the number of prescriptions has intensified the discussion on the use of drugs for treating ADHD among both the general public and professionals. Issues discussed include the risk of providing too much, too little or the wrong kind of care.[11] To answer these questions, it is not sufficient to analyse SHI data alone, since this ignores prescriptions covered by private health insurance. Private prescriptions have been found to be over-represented in an analysis of all prescriptions of methylphenidate in the city of Cologne. Twenty-eight per cent of all prescriptions fell into this category, although only about 10% of all people are privately insured.[12] Moreover, statistics only allow statements to be made on their populations of insured people, and thus cannot be regarded as representative of the population. A further key deficit lies in the fact that prescription data are not necessarily identical to the actual use of a drug, as the latter depends on compliance.[13][14] Beside a genetic disposition, prenatal risk factors such as mother's tobacco smoking[15–17] or alcohol consumption during pregnancy[18] are considered relevant for the pathogenesis of ADHD. The association of these environmental risk factors and ADHD medication use, however, has rarely been addressed. Results of a Swedish study suggest that associations might be confounded by genetic and socioeconomic factors.[15] Sociodemographic characteristics, in turn, like male sex, younger age and not being an immigrant are linked with a greater likelihood of ADHD medication. In addition, education and income level, or the use of medical services have been found to be inversely related to the use of stimulants or atomoxetine in the treatment of ADHD.[19–21] As this information was available from our data, they were considered as risk factors in our analyses. The aim of the present study was to describe the prevalence of the use of ADHD medication—especially stimulants—and to quantify determinants of ADHD medication on the basis of a population-based German representative sample—the German Health and Examination Survey for Children and Adolescents (KiGGS). Based on the literature reviewed above we expect that the use of ADHD medication is associated with younger age, male gender, low socioeconomic status (SES) and not being an immigrant. With regard to the current literature, we wish to explore whether smoking tobacco and drinking alcohol by the mother during pregnancy are related to a higher likelihood for ADHD medication of their offspring in childhood and adolescence. Moreover, the present study aims to assess the extent and the spectrum of drug treatment for ADHD with respect to indication, duration of use, substance group, origin of drugs and perceived ADRs.

MATERIAL AND METHODS
Data source and study population

The KiGGS study was conducted by the Robert Koch Institute between May 2003 and May 2006. The survey's target population was made up of all non-institutionalised children and adolescents aged between 0 and 17 living in Germany. The design, sampling strategy and study protocol have been described in detail elsewhere.[22] Briefly, two-stage sampling procedures were applied. In the first stage, a sample of 167 German municipalities (112 in the former West Germany, 55 in the former East Germany) was drawn which was representative of municipality sizes and structures in Germany. Stratified by sex and age, random samples of children and adolescents aged between 0 and 17 were then drawn from local population registries in proportion to the age and gender structure of Germany's child population. Children and adolescents with a foreign nationality were also included. Children who were currently in institutions such as hospitals, medical and nursing institutions were excluded. The final sample included 17 641 children and adolescents (8985 boys, 8656 girls); the response rate was 66.6%.[23] Of these, 191 study participants who did not take part in the drug-use survey were excluded, resulting in a study population of 17 450 (8880 boys, 8570 girls) available for the present analysis. Parents who decided against a participation in the study were interviewed using a short non-responder questionnaire including sociodemographic and health characteristics. A comparison between responders and non-responders shows that children with mothers with higher educational levels were more likely to participate in the study. In contrast, no substantial differences were observed with regard to the health-related characteristics

such as maternal smoking, maternal body mass index or the parent-rated health status of the child.[23]

The study was approved by the Charité/ Universitätsmedizin Berlin ethics committee and the Federal Office for the Protection of Data. A written informed consent was obtained prior to each interview and examination from children's parents and the children themselves who were over 14 years of age.

Definition of health-related and sociodemographic variables

As described elsewhere in detail,[22] all the children's parents/guardians and all children aged 11 years or older were asked to fill in a standard parents' or children's questionnaire. These questionnaires were used to collect information on socioeconomic data, family backgrounds, parent-rated children's health status, health-related living conditions and behaviour patterns. A family SES score was computed including information obtained from the parents' questionnaire on both parents' educational level and vocational status as well as family net income.[24] After computing a total score from the aforementioned items with a minimum of 3 and maximum of 21 points, study participants were assigned to one of three status groups depending on their individual score.[25] Participants were thus assigned to low, middle or high SES. Family immigration status was assessed using information on nationality, country of birth and year of immigration of both parents. Study participants were classified as having an immigration background if they themselves had immigrated from another country and at least one parent was not born in Germany, or if both parents were immigrants or not of German nationality.[26] Living in East or West Germany as well as living in rural or urban areas was assessed by items concerning the place of residence. Depending on the number of inhabitants, communities were distinguished as rural (<5000), small-size urban (5000−<20 000), medium-size urban (20 000 −<100 000) and metropolitan (100 000 and more). Parents rated the general status of health of their children as 'very good', 'good', 'moderate', 'bad' or 'very bad'. For multivariate analyses, the categories 'moderate' to 'very bad' were pooled due to low cell frequencies. A subject was considered an ADHD case if his or her parents confirmed a lifetime diagnosis from a physician or psychologist. In Germany, the diagnosis of ADHD is not legally restricted to child and adolescent psychiatrists or clinical child psychologists, as in other countries. It is likely, however, that clinical diagnoses are usually assigned by these professional groups. Thus, our measure reflects the clinical judgements of healthcare professionals as reported by parents.[27] Frequency of the mothers' smoking tobacco and alcohol consumption during pregnancy ('regularly', 'from time to time', 'never') was assessed as self-report in the parents' questionnaire. Because in Germany, the use of drugs with the Anatomical Therapeutic Chemical (ATC) code N06BA is legally approved from the age of 6 years on, for the

bivariate and multivariate analyses a classification in the age groups 0–5, 6–10, 11–13 and 14–17 years was chosen. Parents were asked about the utilisation of healthcare services for their child including last visit with a doctor, responses options '< 4 weeks' '1−< 3 months', '3–12 months' and '12+months'.[28]

Assessment of medication use

All survey participants and their parents were asked in advance to bring prescriptions or original medication packages to the examination site to facilitate the investigation and verification of drug use. Use of any medication, including prescribed and non-prescribed drugs, within the last 7 days before their visit in the examination site was documented using a standardised computer-assisted personal drug use interview conducted by a study physician.[29] Drug use was assessed by the following question:

> Has your child taken any drugs in the last seven days? Please also mention the use of any ointments, liniments, contraceptive pills, vitamin and mineral supplements, medicinal teas, herbal medicines or homoeopathic medicines.

Children aged 14 years and older were encouraged to add data on their drug use themselves. All prescribed or over-the-counter (OTC) drugs used in the 7 days before the interview were recorded in the answers to this question in the standardised computer-assisted personal interview (CAPI).

The following information on every drug mentioned by the parents or the children themselves was collected: brand name (as free text), indications (as free text), form of administration (tablets, dragees, drops, ointments, injections, liniments, etc), frequency of intake ('several times a day', 'every day', 'regularly but not daily' or 'every week'), origin of the drug ('prescribed by a doctor', 'prescribed by a non-medical practitioner', 'bought over the counter' or 'obtained from other sources'), duration of use ('<1 week', '1−4 weeks', '1−<12 months' or '1 year or longer') and improvement in the condition(s) treated ('great', 'partial', 'little', 'none' or 'does not apply'). Further, parents and, respectively, the children themselves were asked whether or not the drug used was well tolerated and they were asked to describe the degree of tolerability ('very good/good', 'partial', 'not good' or 'poor'). In addition, a question was asked whether any ADRs were noticed following drug intake ('yes' or 'no'). If the answer was 'yes', the ADRs reported were documented by the study physicians. Specific ATC codes were assigned to all reported medications, and WHO ICD-10 (International Classification of Diseases-10. Revision) codes to the conditions for which the drugs were taken.

Identification of ADHD medication

In the present study, ADHD medication was defined as stimulant and non-stimulant drugs of classes with the

ATC code N06BA, especially with N06BA01 (amphetamine), N06BA02 (dexamphetamine), N06BA03 (methamphetamine), N06BA04 (methylphenidate), N06BA05 (pemoline), N06BA06 (fencamfamin), N06BA07 (modafinil), N06BA08 (fenozolone) and as drugs with the ATC code N06BA09 (atomoxetine).

STATISTICAL ANALYSIS

A weighting factor was computed and used to adjust for deviations in demographic characteristics (age, sex, residence in west or east Germany and level of urbanicity) between the survey population and official population statistics. In the tables, percentages and ORs refer to weighted data, n's are given unweighted. The prevalence rates for ADHD medication use were calculated as follows: children and adolescents with at least one application of a preparation according to our definition of ADHD medication (ATC code N06BA) were defined as users. All other children whose parents completed drug interview and did not report an application according to ATC code N06BA were defined as non-users of these drugs. Descriptive statistics (proportions and 95% CIs) were calculated to analyse characteristics of the study population and to estimate prevalence rates of stimulant and atomoxetine use and associated risk factors. ORs and 95% CIs were obtained from binary logistic regression models. The presence of statistical interactions was examined for all predictor variables in the multivariate model; however, none of the interactions reached statistical significance. Interactions including immigration background did not lead to stable model solutions due to small cell sizes. Group differences were considered statistically significant if a p value was less than 0.05 or if the 95% CIs for two rates did not overlap. All statistical analyses were performed using SPSS statistical software (release 20.0). To adjust for sample clustering effects, the SPSS complex samples module was used for all analyses.

RESULTS
Study population

table 1 lists characteristics of the study sample by gender. The vast majority of boys and girls had a very good or good parent-rated general health status, came from families with no immigration background and resided in former West Germany, and in cities. Nearly half of boys and girls lived in a family with a medium SES, one-quarter, respectively, in families with a low or high SES. About one-third of the children and adolescents reported a visit to a doctor over the past 4 weeks. Less than 10% had not visited a doctor in the past 12 months. More than 80% of the mothers reported that they did not smoke tobacco or drink alcohol during pregnancy at all. There were no significant differences between boys and girls with regard to these characteristics. As previously published, in our sample a parent-reported ADHD diagnosis by a physician or psychologist was significantly more prevalent for boys (7.9%) than for girls (1.8%).[27]

Prevalence and determinants of current ADHD medication

Parents of 158 (0.9%, 95% CI 0.7% to 1.1%) children and adolescents from 0 to 17 years reported ADHD medication throughout the past 7 days, 132 (1.5%; 95% CI 1.2% to 1.8%) boys and 26 girls (0.3%; 0.2% to 0.5%; see table 2). Given a total child and adolescent population aged between 0 and 17 years of 14 828 835 on 31 December 2004 in Germany, these were about 133 460 youth with ADHD medication use by the mean time of our study. Boys thus used these drugs five times more frequently. There were significant differences in the prevalence of use as a function of age, too. Here, the highest prevalence rates were for boys aged 6–13 and girls aged 11–13 years. In each age group, the rates for girls were well below those of boys. Among boys, there was a significant inverse association between an immigration background and the prevalence of stimulant and non-stimulant use. Boys from families with no immigration background were affected more than five times as frequently as boys with an immigrant background (1.7% vs 0.3%). However, there was no evidence of any correlation with SES. A good general health status was more frequently associated with stimulant and non-stimulant use than a very good or moderate to very bad one. Children of mothers who reported regular smoking tobacco displayed significantly higher prevalence rates of ADHD diagnoses than children of mothers who never smoked tobacco (7.5%, 5.3% to 10.7% vs 4.4%, 3.9% to 4.9%). Similarly, regularly drinking alcohol during pregnancy was significantly associated with higher rates of diagnosed ADHD in the offspring (27.5%, 11.1% to 53.4% vs 4.8%, 4.3% to 5.3%, data not shown in table) A similar pattern was observed for ADHD medication use, however, the differences were not statistically significant. It has to be mentioned though that the cell frequency of mothers who reported regularly drinking alcohol during pregnancy and ADHD medication of their child was only two. A visit to the doctor within the last 3 months was associated with a higher prevalence of ADHD medication. Generally, a shorter distance in time to the last visit to the doctor was associated with a higher prevalence of ADHD medication. The differences, however, were not statistically significant. Nevertheless, when using χ^2 test instead of CI analysis there were significant differences with respect to the last visit to the doctor in the total sample as well as in boys (data not shown). This discrepancy in the significance tests is probably due to the small cell sizes. Because of this uncertainty we cannot reliably rule out that there actually are differences. Boys with a diagnosis of ADHD were more likely to being treated with ADHD medication as compared with girls diagnosed with ADHD (21.8% vs 14.8%). The gender differences were statistically significant in the 6-year-old to 10-year-old group (figure 1). The great

Table 1 Sociodemographic and health-related characteristics of survey participants by gender. German Health Interview and Examination Survey for Children and Adolescents 2003–2006 (KiGGS)

	Boys			Girls		
	N**	%*	95% CI	N**	%*	95% CI
Total	8880			8570		
Age group (years)						
0–5	2816	29.2	(28.6 to 29.8)	2794	29.2	(28.5 to 29.9)
6–10	2609	27.1	(26.6 to 27.7)	2490	27.2	(26.6 to 27.4)
11–13	1572	17.3	(17.0 to 17.6)	1468	17.3	(17.0 to 17.7)
14–17	1883	26.4	(25.8 to 27.0)	1818	26.3	(25.7 to 26.9)
Region						
East	2889	16.5	(12.3 to 21.9)	2847	16.5	(12.3 to 21.9)
West	5991	83.5	(78.1 to 87.7)	5723	83.5	(78.1 to 87.7)
Urbanicity						
Rural	1958	17.9	(12.6 to 24.8)	1939	17.9	(12.6 to 24.7)
Small-size urban	2337	27.6	(20.9 to 35.6)	2229	27.2	(20.5 to 35.1)
Medium-size urban	2498	29.0	(22.2 to 37.0)	2475	29.3	(22.4 to 37.2)
Metropolitan	2087	25.5	(19.0 to 33.3)	1927	25.6	(19.1 to 33.5)
Migrant background						
Yes	1350	17.4	(15.4 to 19.6)	1230	16.9	(14.9 to 19.1)
No	7498	82.6	(80.4 to 84.6)	7292	83.1	(80.9 to 85.1)
Missing	32			48		
SES						
Low	2454	27.7	(26.1 to 29.4)	2306	27.3	(25.9 to 28.8)
Middle	4011	45.2	(43.7 to 46.8)	3890	45.7	(44.1 to 47.2)
High	2185	27.0	(25.2 to 29.0)	2181	27.1	(25.2 to 29.0)
Missing	230			193		
Parent-rated subjective health status						
Excellent	3407	38.2	(36.8 to 39.6)	3466	40.1	(38.7 to 41.6)
Good	4759	54.7	(53.2 to 56.1)	4491	53.6	(52.2 to 55.0)
Moderate	567	6.9	(6.2 to 7.6)	486	5.9	(5.3 to 6.6)
Bad	19	0.2	(0.1 to 0.4)	18	0.3	(0.2 to 0.5)
Very bad	7	0.1	(0.0 to 0.2)	5	0.1	(0.0 to 0.1)
Missing	121			104		
Tobacco smoking of the mother during pregnancy						
Regular	386	4.8	(4.2 to 5.4)	402	5.1	(4.5 to 5.9)
From time to time	1080	12.4	(11.6 to 13.3)	1009	12.8	(11.9 to 13.9)
Never	7123	82.8	(81.7 to 83.9)	6901	82.0	(80.8 to 83.2)
Missing	291			258		
Alcohol consumption by the mother during pregnancy						
Regular	10	0.2	(0.1 to 0.3)	15	0.1	(0.1 to 0.2)
From time to time	1122	13.6	(12.2 to 14.3)	1146	14.0	(13.0 to 15.2)
Never	7482	86.6	(85.5 to 87.6)	7183	85.8	(84.7 to 86.9)
Missing	266			226		
Last visit to a doctor						
<4 weeks	2949	32.8	(31.5 to 34.0)	2985	34.7	(33.5 to 35.9)
1–<3 months	2596	29.6	(28.5 to 30.7)	2414	28.5	(27.5 to 29.6)
3–12 months	2448	28.8	(27.6 to 30.0)	2438	29.6	(28.5 to 30.7)
12+months	688	8.8	(8.2 to 9.5)	547	7.2	(6.4 to 8.0)
Missing	199			186		
ADHD diagnosis (physician or psychologist)						
Yes	521	7.9	(7.1 to 8.8)	133	1.8	(1.4 to 2.2)
No	6147	92.1	(91.1 to 92.8)	6538	98.2	(97.8 to 98.6)
Not apply (age)	1397			1373		
Missing	815			526		

%*, weighted; N**, unweighted; ADHD, attention deficit/hyperactivity disorder; SES, socioeconomic status.

majority of the boys and girls only used one preparation; a combination of two drugs of the ATC group N06BA was rarely used (table 2). We did not observe significant differences in the prevalence of ADHD medication between the single years of the survey period (2003–2006) (data not shown in table).

Table 2 Prevalence rates of ADHD medication use (ATC N06BA) by gender. German Health Interview and Examination Survey for Children and Adolescents 2003–2006 (KiGGS)

	Total			Boys		Girls	
	N**	%*	95% CI	%*	95% CI	%*	95% CI
	158	0.9	(0.7 to 1.1)	1.5	(1.2 to 1.8)	0.3	(0.2 to 0.5)
Age (years)							
0–5	0						
6–10	70	1.3	(1.2 to 2.1)	2.3	(1.7 to 3.1)	0.3	(0.1 to 0.7)
11–13	54	1.7	(1.3 to 2.3)	2.7	(2.0 to 3.7)	0.7	(0.3 to 1.4)
14–17	34	0.9	(0.6 to 1.3)	1.4	(0.9 to 2.1)	0.4	(0.1 to 0.9)
Region							
East	54	0.8	(0.5 to 1.2)	1.3	(0.8 to 2.0)	0.2	(0.1 to 0.5)
West	104	0.9	(0.7 to 1.1)	1.5	(1.2 to 1.8)	0.3	(0.2 to 0.5)
Urbanicity							
Rural	30	0.7	(0.4 to 1.1)	1.2	(0.7 to 2.0)	0.1	(0.0 to 0.2)
Small-size urban	41	0.9	(0.6 to 1.3)	1.6	(1.1 to 2.4)	0.1	(0.0 to 0.4)
Medium-size urban	50	0.9	(0.7 to 1.3)	1.4	(1.0 to 1.9)	0.5	(0.2 to 1.0)
Metropolitan	37	1,0	(0.7 to 1.4)	1.6	(1.1 to 2.2)	0.4	(0.2 to 0.9)
Migrant background							
Yes	7	0.4	(0.2 to 0.8)	0.3	(0.1 to 0.8)	0.4	(0.1 to 0.4)
No	151	1.0	(0.8 to 1.2)	1.7	(1.4 to 2.1)	0.3	(0.1 to 0.4)
SES							
Low	42	0.9	(0.6 to 1.2)	1.3	(0.9 to 1.8)	0.5	(0.2 to 1.0)
Middle	81	1.0	(0.8 to 1.3)	1.8	(1.4 to 2.4)	0.2	(0.1 to 0.5)
High	33	0.7	(0.5 to 1.1)	1.2	(0.8 to 1.8)	0.2	(0.1 to 0.6)
Parent-rated subjective health status							
Excellent	29	0.5	(0.3 to 0.7)	0.9	(0.6 to 1.4)	0.1	(0.0 to 0.3)
Good	119	1.2	(1.0 to 1.5)	1.9	(1.5 to 2.4)	0.5	(0.3 to 0.8)
Moderate/Bad/Very Bad†	9	0.8	(0.4 to 1.7)	1.4	(0.6 to 2.9)	0.2	(0.0 to 1.3)
Tobacco smoking by the mother during pregnancy							
Regular	16	1.7	(0.9 to 3.0)	2.4	(1.2 to 4.6)	1.0	(0.4 to 2.7)
From time to time	15	0.8	(0.4 to 1.4)	1.3	(0.7 to 2.4)	0.2	(0.1 to 0.9)
Never	123	0.9	(0.7 to 1.1)	1.5	(1.2 to 1.8)	0.3	(0.1 to 0.5)
Alcohol consumption by the mother during pregnancy							
Regular	2	7.7	(1.9 to 26.5)	14.2	(3.2 to 45.0)		
From time to time	19	0.7	(0.4 to 1.3)	1.0	(0.5 to 1.8)	0.5	(0.2 to 1.4)
Never	134	0.9	(0.8 to 1.9)	1.6	(1.3 to 1.9)	0.3	(0.1 to 0.5)
Last visit to a doctor							
<4 weeks	56	0.9	(0.7 to 1.3)	1.6	(1.1 to 2.3)	0.3	(0.1 to 0.6)
1-<3 months	62	1.3	(1.0 to 1.7)	2.2	(1.6 to 2.9)	0.3	(0.1 to 0.8)
3–12 months	32	0.6	(0.4 to 0.9)	0.9	(0.5 to 1.4)	0.3	(0.2 to 0.7)
12+months	6	0.5	(0.2 to 1.1)	0.8	(0.3 to 1.9)	0.1	(0.0 to 0.6)
ADHD diagnosis (physician or psychologist)							
Yes	142	0.8	(0.6 to 0.9)	1.3	(1.1 to 1.6)	0.2	(0.1 to 0.4)
No	3	0.0	(0.0 to 0.1)	0.1	(0.0 to 0.2)		
Number of medicines (N06BA)							
1	146	0.8	(0.7 to 1.0)	1.3	(1.1 to 1.6)	0.3	(0.2 to 0.4)
2+	12	0.1	(0.0 to 0.1)	0.1	(0.1 to 0.2)	0.0	(0.0 to 0.1)

*%, weighted; N**, unweighted. The sum of each category may not be the total number because of data missing.
†The categories 'Moderate', 'Bad' and 'Very Bad' were collapsed due to low cell frequencies.
ADHD, attention-deficit hyperactivity disorder; ATC, Anatomical Therapeutic Chemical; SES, socioeconomic status.

When potential confounders and risk factors were considered simultaneously, gender, age, city size, immigration status and last visit a doctor showed stable associations with stimulant and atomexetine use (table 3). In addition, a decreasing general health status was significantly associated with increased chances of ADHD medication. However, this was only true for the change from a very good to a good general status of health. As suggested by the bivariate analyses, the associations of mother's smoking tobacco and alcohol consumption during pregnancy remained statistically insignificant. In addition, separate models for boys and girls were run. For boys, the results were similar to the total model. However, the analysis did not result in a stable model solution for girls because only a small number of girls were users of ADHD medication. Further, we examined
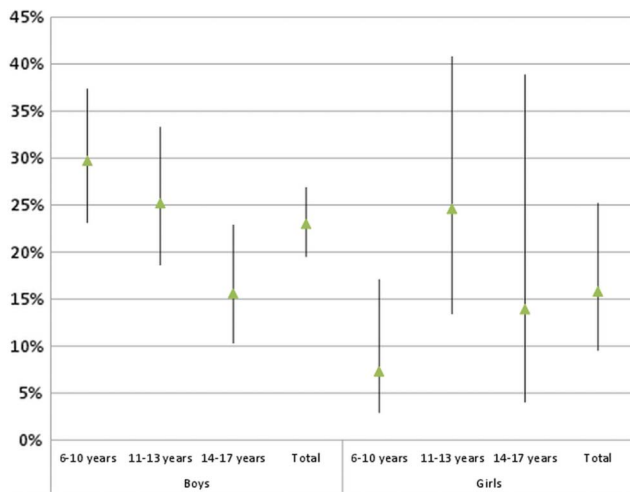
Figure 1 Proportion (% and 95% CI) of attention-deficit hyperactivity disorder (ADHD) medication use in children with ADHD diagnosis (n=145).

in a multivariate binary logistic regression analysis whether youth diagnosed with ADHD *and* ADHD medication differed from those with ADHD *without* medication with respect to all previously used predictors. In summary, we found that after mutual adjustment of all predictors only higher degree of urbanisation, younger age, more recent last visit a doctor uniquely contributed to the model (table 3). Excessive multicollinearity between the predictor variables was not detected. None of the correlations exceeded r=0.42.

Indications and patterns of current ADHD medication use

A total of 171 preparations were mentioned by the 158 children and adolescents currently using ADHD medication. As expected, with 88.9% ADHD (ICD-10; F.90) was the most frequently mentioned indication. Methylphenidate (93.6%) was the most frequently mentioned substance. Atomoxetine and amphetamine-containing drugs were less commonly used (4.1% and 1.8%, respectively) at the time of the survey. As shown in table 4 the use of all drugs was completely based on prescription. Generally, use was mediumterm to long term. Almost one in two drugs (43.9%) had been used for at least 1 year. More than 90% of the parents associated the drug use with an improvement in symptoms, and 88% stated that the tolerability of the preparations was very good or good. Of the 171 drugs used, a total of 21 ADRs (12.3%) were reported. The corresponding percentage for the most frequently mentioned drug, methylphenidate, was 11.9%. In most cases, the reported ADRs were a reduction in appetite (13 cases, 61.9%, data not shown in table). Although the use of ADHD medication is much less common in girls than in boys, the range of indications is almost identical. Hyperkinetic disorder is the main indication for both sexes (94% of the boys and 93% of the girls). Medium-term and long-term use of the drugs outweighs the short-term

application. While it is generally reported for both sexes that the symptoms were considerably improved when using the ADHD medication, the rate of ADRs was twice as high in boys as in girls (13.2 vs 7.4%, table 4). This should be noted, although the difference is not statistically significant. However, the latter is primarily due to the small cell sizes. Significant differences between those with reported ADRs and those without were not observed with respect to age, gender, immigration background, region and degree of urbanisation.

DISCUSSION
Prevalence and determinants

In the nationwide representative KiGGS with more than 17 000 participants, the prevalence of ADHD medication (drugs from the ATC group N06BA) was 0.9%. Boys used these medications 5 times more frequently than girls did. Besides, we found use peaks among the 6-year-olds to 10-year-olds and 11-year-olds to 13-year-olds. Parents of children with no immigration background and parents of children living in large cities reported ADHD medication use significantly more frequently.

The overall prevalence rate reported within our study is much lower than prevalence rates reported from US studies. Yet in the late 1990s and at the beginning of the 21st century, data published by the Medical Expenditure Panel Survey (MEPS) referred to prevalence rates between 2.7% (1997) and 2.9% (2002).[6] After analysing the pharmaceutical data of a private insurance company in the USA, Castle et al[30] stated that 4.4% of all under-19s were prescribed preparations for treating ADHD in 2005. The results of a population-based regional longitudinal study in Israel revealed a prevalence of methylphenidate prescription of 1.1% in girls and 3.8% in boys of school age.[7] A similar level of stimulant prescription and use is reported by analyses of population-related pharmacy data[31] and representative household surveys[32] in Australia. In contrast, prevalence rates reported for Western European and Scandinavian countries are markedly lower. A national cohort study in Sweden conducted in 2005 shows a low level of ADHD medication comparable with our study.[33] [34] Study results from the Netherlands[35] and France[36] as well as an analysis of data of one of the biggest health insurances in Germany[37] also indicate a lower use of stimulants in Western Europe than in the USA that is comparable with the results from our study. Significant differences in the prevalence of ADHD medication between the single years of the survey period of our study were not observed. Based on health insurance data Schubert et al[37] report a doubling in prevalence of ADHD medication use from 0.54% to 1.06% between 2000 and 2007. The prevalence in our study had an average value of 0.9% from the years 2003 to 2006 within this range. Differences in study design and the date when the survey was carried out must be taken into account when comparing our data with published results. A growing

Table 3 Multivariate associations between ADHD medication and risk factors in youth (total sample and youth with ADHD diagnosis only) (OR and 95% CI)

	All children N=11,142* OR (95% CI)	p Value	Children with ADHD diagnosis N=586† OR (95% CI)	p Value
Gender		<0.001		0.171
Boys	5.16 (3.15 to 8.47)		1.50 (0.84 to 2.7)	
Girls	1 (Ref.)		1 (Ref.)	
Age (years)		0.018		0.036
6–10	1.60 (0.94 to 2.72)		2.04 (1.09 to 3.81)	
11–13	2.24 (1.28 to 3.94)		2.19 (1.16 to 4.11)	
14–17	1 (Ref.)		1 (Ref.)	
Region		0.257		0.136
East	1 (Ref.)		1 (Ref.)	
West	1.32 (0.83 to 2.12)		1.41 (0.90 to 2.23)	
Urbanicity		0.014		
Rural	1 (Ref.)		1 (Ref.)	0.127
Small-size urban	1.60 (0.81 to 3.18)		1.60 (0.84 to 3.04)	
Medium-size urban	1.78 (0.94 to 3.41)		1.96 (1.07 to 3.60)	
Metropolitan	2.18 (1.13 to 4.22)		2.02 (1.03 to 3.98)	
Migrant background		0.008		0.727
Yes	1 (Ref.)		1 (Ref.)	
No	3.06 (1.34 to 6.99)		1.22 (0.39 to 3.81)	
SES		0.500		0.128
Low	1.29 (0.75 to 2.21)		0.52 (0.27 to 0.98)	
Middle	1.33 (0.82 to 2.14)		0.64 (0.35 to 1.19)	
High	1 (Ref.)		1 (Ref.)	
Parent-rated subjective health status		0.018		0.127
Excellent	1 (Ref.)		1 (Ref.)	
Good	1.91 (1.18 to 3.08)		1.22 (0.68 to 2.19)	
Moderate/Bad/Very Bad	1.18 (0.51 to 2.74)		0.53 (0.21 to 1.33)	
Tobacco smoking during pregnancy		0.221		
Regular	1.64 (0.85 to 3.18)		0.46 (0.16 to 1.28)	0.322
From time to time	0.78 (0.41 to 1.48)		0.71 (0.32 to 1.57)	
Never	1 (Ref.)		1 (Ref.)	
Alcohol consumption during pregnancy		0.427		0.675
Regular	3.16 (0.27 to 37.01)		0.82 (0.06 to 11.64)	
From time to time	0.77 (0.44 to 1.25)		1.13 (0.09 to 14.66)	
Never	1 (Ref.)		1 (Ref.)	
Last visit to a doctor		<0.001		0.025
< 4 weeks	3.18 (1.29 to 7.85)		2.07 (0.77 to 5.54)	
1–< 3 months	3.59 (1.45 to 8.90)		2.96 (1.12 to 7.77)	
3–12 months	1.35 (0.52 to 3.52)		1.29 (0.44 to 3.79)	
12+months	1 (Ref.)		1 (Ref.)	
Nagelkerke pseudo-R^2	10.6%		11.7%	

Italicised values indicate significant results.
*6308 subjects are missing due to list-wise deletion.
†68 subjects are missing due to list-wise deletion.
ADHD, attention-deficit hyperactivity disorder; SES, socioeconomic status.

trend in prescription and use can be observed over the past few decades.[10] [30] [37] Furthermore, the prescription and use of ADHD drugs is highly dependent on gender and age. Studies looking at different populations in terms of age and gender and carried out at different times will thus arrive at different prevalence estimates for these reasons alone. Another decisive factor is the period over which the use of a drug is observed. If data collection covers a period of 7 days, as in our study, any interruption of intake can lead to prevalence rates being underestimated. On the other hand, shorter periods reduce recall bias. However, a three-country comparison carried out by Zito et al[38] shows that the prevalence of stimulant prescription in children and adolescents in the USA (4.29%) is much higher than the corresponding rates in the Netherlands (1.18%) and Germany (0.71%) even when these differences in study design are largely excluded. The lower prevalence rate in western

Table 4 ADHD medication by indication (ICD-10.Rev.), substance group, origin, self-rated improvement of conditions treated, tolerance, duration of use and perceived adverse drug reactions (ADRs)

	Total		Boys		Girls		
	N*	%*	N*	%*	N*	%*	p Value
	171	100	144	100	27	100	
Indications (ICD 10.Rev.)							0.219
Unknown	1	0.6	1	0.7			
Severe depressive episode without psychotic symptoms (F32.2)	1	0.6	1	0.7			
Specific reading disorder F81.0	1	0.6	1	0.7			
Disturbance of activity and attention (F90.0)	149	87.1	125	86.8	24	88.9	
Hyperkinetic disorder, unspecified (F90.9)	3	1.8	3	2.1			
Combined vocal and multiple motor tic disorder (de la Tourette) (F95.2)	1	0.6	1	0.7			
Other specified behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F98.8)	3	1.8	3	2.1			
Epilepsy, unspecified (G40.9)	1	0.6	0		1	3.7	
Malaise and fatigue (R53)	11	6.4	9	6.3	2	7.4	
Medicine (ATC code)							0.826
Amfetamine (N06BA01)	3	1.8	2	1.4	1	3.7	
Dexamfetamine (N06BA02)	1	0.6	1	0.7			
Methylphenidate (N06BA04)	160	93.6	135	93.8	25	92.6	
Atomoxetine (N06BA09)	7	4.1	6	4.2	1	3.7	
Origin of the medicine							
Prescription	171	100	144	100	27	100	
Duration of use							0.344
<1 week	11	6.4	9	6.3	2	7.4	
1−<4 weeks	22	12.9	21	14.6	1	3.7	
1−<12 months	63	36.8	50	34.7	13	48.1	
>=1 year	75	43.9	64	44.4	11	40.7	
Missing							
Self-rated improvement of conditions treated							0.944
Great	98	59.4	83	57.6	15	55.6	
Partial	57	34.5	48	33.3	9	33.3	
Little	6	3.6	5	3.5	1	3.7	
Missing	10		8		2		
Tolerance for the medicine							0.860
Very good/good	151	88.8	126	87.5	25	92.6	
Partial	16	9.4	14	9.7	2	7.4	
Not good	1	0.6	1	0.7			
Poor	2	1.2	2	1.4			
Missing	1						
Perceived ADR	21	12.3	19	13.2	2	7.4	0.317
Amfetamine (N06BA01)	1	0.6	1	0.7			
Methylphenidate (N06BA04)	19	11.1	17	11.8	2	7.4	
Atomoxetine (N06BA09)	1	0.6	1	0.7			

*N and % unweighted.
ADHD, attention-deficit hyperactivity disorder; ATC, Anatomical Therapeutic Chemical; ICD, International Classification of Diseases.

Europe (including Germany) and above all the Scandinavian countries is thought to be caused by more restrictive legislation on the prescription of stimulants[11 39]

Most international studies report boys to be much more likely to be treated with stimulants than girls and that there is a marked increase when children reach school age.[7 30–36] This corresponds well with the prevalence rates that we found in our study and consistently, in our sample, boys were found to be four times more likely to be diagnosed with ADHD than girls.[27] Results from the USA[40] and from Canada[41] show that although ADHD is diagnosed more frequently among children from socially deprived families, children from such families receive a corresponding drug therapy less frequently. In our study, we found no significant differences for SES concerning ADHD medication, although children diagnosed with ADHD were twice as prevalent in families with low SES in our sample, too.[27] This suggests that children from families with low SES may be disadvantaged in receiving adequate drug therapy when

being diagnosed with ADHD. In contrast, however, a lower educational level of a child's mother and the status of being a 'single parent' and a 'social welfare recipient' proved to be significant determinants of a greater likelihood of ADHD medication in a Swedish cohort study.[33] The fact that we found youth living in large urban centres to be more frequently using ADHD medication may be due to differences in access to healthcare services in rural versus urban regions. This is supported by the fact that we did not find significant differences in the prevalence of diagnosed ADHD with respect to the degree of urbanisation.[27] When comparing children with ADHD diagnosis with and without ADHD medication in an additional analysis, we found that differences in the degree of urbanisation were still present even after adjusting for potential confounders. With respect to the association of ADHD medication use and immigration background our results correspond to those of various studies.[9–21 42] In a population-based study of the prescription data of the largest health insurance company in the Netherlands, Wittkampf et al[42] report that ADHD medication is less likely to be prescribed to children of Turkish and Moroccan families than to Dutch boys and girls. This may either point to differential thresholds to healthcare services for immigrants or may even be due to culturally altered attitudes towards symptoms of ADHD. Olfson et al[19] suggest that cultural factors, rather than economic factors, may explain the lower prevalence of ADHD treatment in racial or ethnic minorities. Also, in our sample we found that children from families with immigration background were less likely to be diagnosed with ADHD than children from non-immigrant families. Nevertheless, the prevalence of clinically relevant ADHD symptoms was far higher in immigrant children,[27] which argues against a 'healthy immigrant' effect.

In our study, most parents of children with ADHD medication rated the general status of health of their child as good but not excellent. This is plausible as on the one hand stimulant medication is known to significantly improve ADHD symptoms which may result in a better subjective health. On the other hand, the fact that their child is dependent on a long-term medication may not encourage parents to rate general health status as excellent.[43]

Risky health behaviours during pregnancy including regularly smoking tobacco and regularly drinking alcohol during pregnancy are known to occur more frequently in socially deprived families.[15 18] In multivariate analysis, however, we did not find any significant associations between those prenatal risk factors and ADHD medication. This corresponds to the results of Lindblad and Hjern who found that the associations of maternal tobacco consume during pregnancy and ADHD medication in the offspring were largely explained by confounding by genetic and socioeconomic factors.[15]

Treatment of ADHD with stimulants and atomoxetine
In our study, about one-fifth of all children and adolescents with diagnosed ADHD were treated with stimulants and atomoxetine. This rate is well below figures from the USA; more than half (50–60%) of the affected children receive appropriate medication.[19 29 30] Boys with ADHD diagnosis have a higher prevalence of drug therapy as ADHD-affected girls. In our sample, the ratio of boys to girls with a parent-reported ADHD diagnosis and treatment with stimulants and atomoxetine was 1.5:1. However, these differences were statistically significant only in children of primary school age. Derks et al[44] suggest that higher ADHD medication use rates in boys may be due to differential behavioural ratings by teachers in the schools. They observed that teachers reported higher problem scores of attention and aggression for boys with ADHD than for ADHD-affected girls in the school setting, whereas mothers reported similarly high levels in boys and girls with ADHD at home. The observed increase in the rate of ADHD medication use in primary school age aligns with the increase of diagnosed ADHD in our sample[27] and is likely explained by the fact that in Germany the use of ADHD medication is licenced only for the age 6 years and above. A further explanation for the increase of ADHD diagnoses and ADHD medication use with the beginning of school is also due to increased demands (eg, sitting still) from the preschool to the school setting, when symptoms of ADHD impact more strongly.

Indications and patterns of current ADHD medication use
Among all preparations methylphenidate was used most frequently, that is, in almost 94% of cases. Consistent with other studies,[34 35 43 45] our results indicate that methylphenidate is most frequent among the drugs used. The improvement in ADHD symptoms under medication reported in KiGGS confirms findings by Thorell and Dalström in a survey of Swedish children.[43] With a proportion of 12.3%, however, parents reported for more than 1 in 10 children and adolescents with ADHD medication an ADR, in particular for methylphenidate. Against the background of a generally low overall prevalence of ADRs in our sample, these effects after ADHD medication are nevertheless among the ones most frequently mentioned.[46]

Strengths and limitations
KiGGS is a population-based study and due to its representative design it allows generalisations to be made on the use of ADHD medication in children and adolescents in Germany. The survey of drug use together with the collection and measurement of health-related data allows a representative description of ADHD medication in the German child and adolescent population under everyday conditions and regardless of the use of medical services. The fact that information on drug use relates to the last 7 days does have a limiting effect, however. Although, on the one hand, this reduces the likelihood of a recall bias, on the other it can lead to misclassifications as users when children and adolescents who have interrupted intake at the time of the survey reported

that they are not currently taking any medication. The data on ADHD medication use are based on self-reports by study participants or their parents. Drug use that is consciously or unconsciously concealed can thus lead to an underestimation of the true use of ADHD medication. The particular focus of the KiGGS study as a population-representative cross-sectional health survey is to identify risk groups and describe any risk constellations. Cause−effect relations cannot be generated on the basis of these cross-sectional data. As the KiGGS study is recently continued as cohort study, this will be made possible for the first time in 2012 when the field work of the next wave is completed.

CONCLUSIONS

The results of the KiGGS study representative for the German child and adolescent population show a prevalence rate of stimulant use that is considerably lower than the published prevalence rates from the USA, but comparable with those of western European and Scandinavian countries. The data on higher prevalence in boys and an increase in pharmacotherapy when children reach school age are comparable in all published studies. The associations with living conditions (large urban centres, immigrant background) which were confirmed in multivariate analysis potentially point to differences in access to healthcare services and culture-specific differences in attitudes towards ADHD. Further clues on the determinacy of ADHD medication, on efficacy and long-term results will be provided by the data from the KiGGS cohort study.

Author affiliations
[1]Department of Epidemiology and Health Reporting, Robert Koch Institute, Berlin, Germany
[2]Department of Child and Adolescent Psychiatry, Johannes Gutenberg-University, Mainz, Germany

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