ORIGINAL ARTICLE

The Changing Prevalence of Attention-Deficit/Hyperactivity Disorder and Methylphenidate Prescriptions

A Study of Data From a Random Sample of Insurees of the AOK Health Insurance Company in the German State of Hesse, 2000–2007

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SUMMARY

Background: The goal of this study is to assess changes in the prevalence of attention-deficit/hyperactivity disorder (ADHD) and methylphenidate prescriptions over the period 2000 to 2007 on the basis of data from a German statutory health insurance carrier.

Methods: In a cross-sectional study, we analyzed data from a random sample of insurees of the AOK health insurance company in the German state of Hesse for the years 2000 to 2007. Per calendar year, 50 000 to 63 000 children and adolescents were retrospectively observed with respect to the documentation of ADHD diagnosis (ICD-10 diagnosis F90) and the prescribing of methylphenidate (ATC: N06BA04).

Results: In 2007, the overall prevalence of ADHD in all age groups (0–18 years) was 2.21% (95% CI: 2.09–2.34). This figure was 45% greater than the corresponding figure for the year 2000. The prevalence increased by a larger amount among girls aged 6 to 18 years than among boys in the same age group (+69% vs. +53%). In 2007, 1.06% (95% CI: 0.98–1.16) of the children/adolescents received at least one prescription for methylphenidate; this was a 96% increase over the prescription rate for 2000. A comparison of the two years 2000 and 2007 reveals a clear prevalence shift towards the older age groups, as well as an 82% increase in the average number of daily doses per recipient. Outpatient departments of child and adolescent psychiatry initiated more treatments in 2007 than in 2000.

Conclusion: The 1% prevalence of methylphenidate use among children and adolescents that was found in this study is the same as that reported in other European countries, such as Switzerland, the Netherlands, and Norway. A drawback of our study is its limitation to a single insurance carrier in a single region. Nonetheless, data of this type are useful for monitoring. The findings suggest further issues worth studying, e.g., off-label use or the indications for treatment in older age groups.

The volume of methylphenidate prescriptions in Germany is well documented by data contained in the Medications Index (*Arzneimittelindex*) of the statutory health insurance carriers (*Gesetzliche Krankenversicherungen*, GKV) (1). A marked increase in the number of methylphenidate prescriptions per person first became evident in the early 1990s, although the overall volume at that time was still low. Since 1997, the volume of prescriptions has increased nearly tenfold; in 2007, 45.7 million daily doses of methylphenidate were prescribed (1). Some of this increase can be accounted for by the issuance, by the German Society of Child and Adolescent Psychiatry (*Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie*), of recommendations for methylphenidate treatment in their first published guidelines on the treatment of attention deficit/hyperactivity disorder (ADHD) (2). Nevertheless, the increase is so large that other factors are surely at work which require attention.

Understandably, this development has provoked debate, among specialists and the general public, regarding both the disease entity ADHD itself and the indications for its treatment. One consequence of this debate was a change in the drug approval conditions for methylphenidate, which went into effect on 1 September 2009. Methylphenidate can now be prescribed in Germany only if other therapeutic measures have yielded inadequate benefit. Moreover, any such treatment must be under the supervision of a specialist in behavioral disorders. It was also in 2009 that an expert advisory panel, in its detailed consideration of hyperkinetic disorder (HKD) pointed out that the multimodal treatment approach is still inadequately implemented.

It has been stated that multidisciplinary research is needed on the etiology of the condition and the development of measures to prevent it (3). Epidemiological data on the frequency of HKD/ADHD and the treatment of patients with these disorders are needed which will serve as the basis for a critical assessment of secular trends. In this article, a continuation of our earlier work on the subject (4, 5), we give estimates of the following for the year 2007:

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- The frequency of treatment for HKD
- The percentage of children and adolescents that are under treatment with methylphenidate.

These results are compared with the corresponding figures for the year 2000. The age- and sex-specific changes that our study revealed, as well as the changes in quantity prescribed per person, are of particular interest.

Materials and methods

Database and study population

The “Statutory Health Insurance sample (SHI) AOK Hesse, KV Hesse”—a 18.75% random sample of AOK insurees—served as our database. Persons belonging to the random sample at the outset of data collection (1 January 1998) who later dropped out were replaced by others, in order to keep the sampling ratio constant over time. For each year in which data were collected, data are available for the entire course of the year on a total of 270 000 to 330 000 insurees, including 50 000 to 63 000 children and adolescents up to age 18.

In 2007, about one-quarter (27%) of the population of the German federal state of Hesse was insured by AOK. The percentage of persons aged 18 and under varied, depending on the year, from 18.4% to 19.6% and was thus comparable to the percentage in the overall population of Hesse (18.5%), with a comparable sex distribution (51% boys, 49% girls).

Data from the random sample of insurees are available in pseudonymized fashion. In other words, data on any individual person can be traced over the entire time period of data collection, even though the identity of that person cannot be determined. In the present study, we made use of the following data:

- Master data such as age, sex, and time insured
- Outpatient medical diagnoses (listed for each three-month period)
- Prescription data (drug identification number, date of prescription), including the specialty of the physician who wrote the prescription.

The database is extensively described elsewhere (6).

Identification of patients

A patient was assumed to have been under treatment for HKD/ADHD if an inpatient or outpatient diagnosis with the ICD-10 code F90 had been assigned. Diagnoses that were qualified as “suspected” or “excluded” were not counted. Our estimate of the prevalence of treatment with methylphenidate took account of all insurees who, in the year in question, were given at least one prescription for methylphenidate. Prescriptions for methylphenidate were identified in a drug database created specifically for this research project on the basis of the anatomic-therapeutic-chemical (ATC) classification code N06BA04. The total amount prescribed was determined from the number of prescribed daily doses. One defined daily dose (DDD) of methylphenidate equals 30 mg, by international convention (e1).

Statistical analysis and review of the literature

The data were entered into a database (MSSQL-Server 2008 under Windows Server 2003) and evaluated with the aid of SQL and the statistical program package SAS for Windows, Release 9.2.

Frequency estimates are reported as percentages. 95% confidence intervals (95% CI) relating to these percentages were calculated with the aid of Wilson’s score intervals (e2). Changes in prevalence from 2000 to 2007 are reported as relative changes. For example, the prevalence of HKD among 10- to 14-year-olds rose from 1.66% in 2000 to 3.35% in 2007; the percentage change is therefore $(3.35 - 1.66) / 1.66 \times 100\%$, or +102% (rounded to the nearest whole number).

To compare our findings with those of other studies, we selectively searched the literature (Medline and reports of the statutory health insurance carriers) up to July 2009 for all studies based on prescribing data over a time span that included the years 2000 to 2007.

Results

In 2007, 2.21% (95% CI: 2.09–2.34) of persons up to age 18 (all age subcategories) were treated for HKD (boys: 3.39%, 95% CI: 3.18–3.63; girls: 0.97%, 95% CI: 0.86–1.11) (Table 1). The female-to-male ratio was 1 : 3.5. The diagnosis was relatively rare in adulthood (2007: fewer than 0.1% of persons over age 18; data not shown). The diagnosis HKD was coded as a reason for treatment just under 1.5 times as frequently in 2007 as in 2000. Among children and adolescents aged 6 to 18, the relative increase was +53% for boys and +69% for girls (data not shown). The greatest increase (+297%) was among 15- to 18-year-olds.

In 2007, 1.06% (95% CI: 0.98–1.16) of persons up to age 18 received at least one prescription for methylphenidate, with a female-to-male ratio of 1 : 4.4. Methylphenidate was not prescribed to any children under age 6, although some children in this age group were documented as having been treated for a diagnosis of HKD. Thus, methylphenidate was prescribed only for children of school age. 10- to 14-year-olds had the highest prevalence of treatment (Table 2). The overall treatment prevalence nearly doubled from 2000 to 2007; among 15- to 18-year-olds, the treatment prevalence indeed rose more than five-fold over this period, albeit from a low baseline. In the combined age group of 6- to 18-year-olds, the prevalence of methylphenidate prescriptions among boys rose from 1.23% (95% CI: 1.10–1.38) in 2000 to 2.22% (95% CI: 2.03–2.44) in 2007, corresponding to a relative rise of +80.5%. Among girls in the same age group over the same time period, there was a disproportionate relative rise of +188.9%, from 0.18% (95% CI: 0.14–0.26) in 2000 to 0.52% (95% CI: 0.43–0.64) in 2007 (data not shown).

The Figure displaying the prevalence of hyperkinetic disorder and methylphenidate prescriptions by age in 2000 and 2007 clearly shows increases in both the rate of diagnosis of HKD and—to an even larger extent—the prescription of methylphenidate in childhood and adolescence. The mean age of persons taking methylphenidate (up to age 18) rose from 10.3 to 11.9

TABLE 1

The percentage of children and adolescents (≤ 18 years old) with HKD in 2000 and 2007, grouped by sex and age

		Prevalence of treatment for HKD (%)				
Sex	Age (years)	2000		2007		Relative change from 2000 to 2007 (%)
		Percentage (%)	95% confidence interval	Percentage (%)	95% confidence interval	
Male	<5	0.95	0.77–1.25	0.66	0.50–0.98	– 31
	5 to 9	4.38	3.99–4.85	4.48	4.04–5.04	+ 2
	10 to 14	2.67	2.39–3.03	5.22	4.77–5.77	+ 96
	15 to 18	0.48	0.36–0.70	2.18	1.88–2.60	+ 354
	All ages	2.31	2.16–2.49	3.39	3.18–3.63	+ 47
Female	<5	0.51	0.39–0.75	0.19	0.13–0.42	– 63
	5 to 9	1.3	1.10–1.60	1.54	1.29–1.90	+ 18
	10 to 14	0.57	0.46–0.77	1.35	1.13–1.68	+ 137
	15 to 18	0.21	0.15–0.40	0.56	0.43–0.81	+ 167
	All ages	0.68	0.60–0.79	0.97	0.86–1.11	+ 43
Both sexes	<5	0.73	0.61–0.91	0.43	0.33–0.61	– 41
	5 to 9	2.88	2.65–3.16	3.04	2.77–3.36	+ 6
	10 to 14	1.66	1.49–1.86	3.35	3.09–3.67	+ 102
	15 to 18	0.35	0.27–0.48	1.39	1.22–1.62	+ 297
	All ages	1.52	1.43–1.62	2.21	2.09–2.34	+ 45

HKD, hyperkinetic disorders; ICD-10 diagnosis F90, without the supplementary designation "suspected" or "excluded"

TABLE 2

The percentage of children and adolescents (≤ 18 years old) for whom methylphenidate was prescribed in 2000 and 2007, grouped by sex and age

		Prevalence of treatment for HKD [%]				
Sex	Age (years)	2000		2007		Relative change from 2000 to 2007 (%)
		Percentage (%)	95% confidence interval	Percentage (%)	95% confidence interval	
Male	<5	0	–	0	–	
	5 to 9	1.4	1.20–1.69	1.44	1.21–1.79	– 3
	10 to 14	1.55	1.34–1.83	3.19	2.84–3.64	+ 106
	15 to 18	0.27	0.20–0.46	1.51	1.27–1.87	+ 459
	All ages	0.92	0.82–1.03	1.7	1.56–1.88	+ 85
Female	<5	0.02	0.02–0.14	0	0.01–0.15	– 100
	5 to 9	0.2	0.15–0.35	0.45	0.34–0.69	+ 125
	10 to 14	0.23	0.17–0.37	0.74	0.59–1.00	+ 222
	15 to 18	0.05	0.03–0.18	0.24	0.17–0.43	+ 380
	All ages	0.14	0.11–0.19	0.39	0.33–0.49	+ 179
Both sexes	<5	0.01	0.01–0.07	0	0.01–0.08	– 100
	5 to 9	0.82	0.71–0.98	0.96	0.82–1.15	+ 17
	10 to 14	0.91	0.79–1.06	2.01	1.81–2.26	+ 121
	15 to 18	0.16	0.12–0.26	0.89	0.76–1.08	+ 456
	All ages	0.54	0.49–0.60	1.06	0.98–1.16	+ 96

Methylphenidate: ATC N06BA04

The percentage of insureds given the diagnosis of hyperkinetic disorder (HKD) and the percentage of insureds receiving methylphenidate prescriptions, according to age and year (2000, 2007)

years over this time period. In other words, the distribution of individuals taking this drug shifted, between 2000 and 2007, toward adolescents and young adults.

An overview of the prevalence of treatment with methylphenidate and of the average number of prescribed daily doses for 6- to 18-year-olds, shown in Table 3, reveals that the latter figure rose by 252% from 2000 to 2007. This is evidently due not only to the larger number of children and adolescents for whom methylphenidate was prescribed (+93%), but also to a marked rise in the mean number of defined daily doses (DDD) prescribed per patient, from 114 in 2000 to 208 in 2007 (+82%). An increase was seen in all age groups. In comparison to prescribing patterns in 1999 and 2000 (7), the percentage of children and adolescents who received only a single prescription rose slightly, from 15.5% to 17.4% in 2007. Although it was also the case in earlier years, just as in 2007, that more than half of all children (52%) in their first year of treatment received prescriptions for a prolonged time period (more than 280 days), only 8% were prescribed a sufficient amount for continuous treatment with one DDD per day; by 2007, this percentage rose to 16%. In 2007, 14.4% of 6- to 18-year-olds taking methylphenidate received more than 400 DDD in the course of the year, and 1.5% received more than 730 DDD (a figure corresponding to 60 mg of methylphenidate per day).

The role of prescribing physicians also changed from 2000 to 2007: pediatricians were less commonly the initial prescribers of methylphenidate in 2007 than in 2000 (37.7%, compared to 48.2%), and the same is true of general practitioners (10.8%, compared to 12.8%). The percentage of initial prescriptions by psychiatrists (including child and adolescent psychiatrists) or by free-standing or hospital-based outpatient psychiatric clinics changed inappreciably over this time period (from 30.5% to 31.1%, and from 6.4% to 6.6%, respectively). On the other hand, the initiation of treatment in outpatient child and adolescent psychiatric clinics rose markedly, from 3.5% to 12.3%.

Discussion

This study, based on data that were routinely obtained by a health insurance carrier, reveals a secular trend in the prevalence of HKD as well as in the prevalence of methylphenidate prescriptions. It is evident from the findings presented here that not every diagnosis of HKD leads to the prescription of medication, and, most importantly, that no off-label treatment is being provided to children under age 6. The nature of the database enabled the study to be performed without selection bias (as would have arisen, for example, in a study based on data from medical practices or hospitals) and without any recall or refusal bias. One limitation of this study is that it is based on the data of a single type of health insurance carrier in a single region in Germany. The study determined that the overall prevalence of treatment in 2007 was 1.1%; this figure is considerably lower than the nationwide estimate of 1.7% that was derived from insureds of the GEK health insurance carrier (8). We can only speculate whether this difference is accounted for by the GEK insureds themselves (e.g., because they, or their parents, are better informed about treatment options), or by the persons treating them (the total volume of drug prescriptions per capita is known to be lower in Hesse than in the country as a whole). Our estimate of the prevalence of treatment with methylphenidate is based only on prescriptions issued in the framework of the statutory health insurance system and is therefore an underestimate, as it takes no account of private prescriptions or of physicians' drug samples handed out to patients without a prescription. The findings of Bessou et al. (9) are relevant in this connection: their analysis of all prescriptions filled in pharmacies in Cologne revealed that the percentage of private prescriptions was higher than would have been expected from the percentage of privately insured patients. Like all studies based on routine data, this study permits no conclusion about the correctness of indications for treatment, or whether the medication was actually taken as prescribed.

Our prevalence estimates cannot be directly compared with estimates based on other studies that were designed according to other methods, not only because of the varying criteria that are used to define the condition in question, but also because of the varying time

TABLE 3

Methylphenidate prescriptions for 6- to 18-year-olds in the years 2000 to 2007

Year	Persons receiving methylphenidate		Insurees with methylphenidate		Prescribed daily doses of methylphenidate (DDD)			
					Per person receiving methylphenidate		Per 100 insurees	
	Percentage of girls (%)	Mean age (years)	Percentage (%)	Change (2000 level = 100%)	Number	Change (2000 level = 100%)	Number	Change (2000 level = 100%)
2000	12.2	10.3	0.72	100	114	100	82	100
2001	16.8	10.5	0.86	119	120	105	103	126
2002	14	10.8	0.94	131	121	106	113	138
2003	14.9	11.2	1.02	142	134	118	136	166
2004	16.7	11.3	1.06	147	152	133	162	198
2005	19.1	11.7	1.11	154	184	161	205	250
2006	18.4	11.8	1.3	181	193	169	250	305
2007	18.2	11.9	1.39	193	208	182	289	352

methylphenidate: ATC N06BA04

spans used for the estimation of prevalence. The German Health Interview and Examination Survey for Children and Adolescents (*Kinder- und Jugendgesundheitssurvey*, KiGGS) yielded an estimate of 4.8% for the lifetime prevalence of ADHD for children and adolescents aged 3 to 17; this figure is higher than the 12-month prevalences found by the authors (10). Similarly, Schlander and colleagues (2007) estimated the 12-month prevalence of HKD, as defined by the ICD-10 diagnosis code F90.0, in the year 2003 on the basis of data from statutory health insurance carriers in northern Baden (a region in the state of Baden-Württemberg); they arrived at figures of 7.2% for boys and 2.7% for girls aged 7 to 12 (11). Our own study's estimates of the administrative treatment prevalence of HKD (F90) in 2003 among 7- to 12-year-olds are considerably lower: 5.8% for boys, 1.7% for girls, and 3.8% for the two sexes combined. Regional variations in treatment are to be expected, as has been shown with other data from the statutory health insurance carriers (e3). The KiGGS defined cases of ADHD with the aid of standardized instruments and arrived at a prevalence estimate of 3.5% among 7- to 10-year-olds, which is comparable to the finding of the present study (12). Unfortunately, none of the studies mentioned, other than our own, included data on the prevalence of treatment with methylphenidate or other stimulants.

Our estimate of the prevalence of treatment with methylphenidate, derived from a random sample of insurees of AOK Hesse for the year 2007, is markedly higher than the corresponding estimate for 2000, as was to be expected in view of the nationwide increase of methylphenidate prescriptions over this time period. The prevalence that we found is, however, still less than the estimated prevalences that have been reported in other countries, such as the USA, Iceland, and Israel (Table 4). The treatment of children and adolescents

with methylphenidate has been studied in many countries and has been described as an important public health problem in nearly all of them, with the exception of France. While the data from Germany and a few other European countries indicate a marked rise since the mid-1990s, Zuvekas et al. did not find any such rise in the USA, where the use of stimulants did not change significantly from 1997 to 2002 (13). In the USA, however, methylphenidate is used much more commonly than in many European countries: in Switzerland (14), the Netherlands (15), and Norway (16), for example, the prevalence of treatment with methylphenidate among children and adolescents has been estimated at about 1%, on the basis of data sources comparable to those used for the present study. A French study (21) yielded a remarkably low prevalence estimate. The authors mentioned possible underdiagnosis as a potential reason for this, but they did not point out the stratification bias that may well have resulted from their studying a predominantly academic clientele.

The present study reveals an increase in the diagnosis of HKD (i.e., coding as a treatment indication) and two noteworthy secular trends:

- An increase in the average daily dose of methylphenidate
- An increase in the frequency of treatment with methylphenidate among adolescents.

Our analysis shows that continuous, long-term treatment has become more common since 2000. In an earlier study, we found that only a small number of patients were treated over a prolonged period of time with a single recommended daily dose (7); perhaps prescribing patterns in Germany have, in the meantime, come closer to the internationally recognized therapeutic standards (see also the treatment recommendations of the German Society of Child and Adolescent Psychiatry [*Deutsche Gesellschaft für Kinder- und*

TABLE 4

The prevalence of treatment with stimulants/methylphenidate in different countries

Author, year of publication, country, reference number	Database / source of data	Age group	Prevalence (95% CI)
Zuvekas et al. 2006, USA (13)	Medical Expenditure Panel Survey 1997–2002 (Questionnaire and data from pharmacies) (MEPS public use prescription file)	0–19 years	Stimulants (2002): 2.9% (95% CI: 2.5–3.3), <6 years: 0.3%, 6–12 years: 4.8%, 13–19 years: 3.2%
Habel et al. 2005, USA (17)	Data of the Kaiser Permanente health insurance system (1996–2000)	2–18 years	Stimulants: 2000: 1.93% (95% CI: 1.90–1.96)
Preen et al. 2007, Western Australia (18)	Data from pharmacies (2004)	3–17 years	Stimulants (2004): 3–17 years: 2.4% Dexamphetamine: 1.6% MPH: 0.89%
Zoëga H et al. 2007, Iceland (19)	Prescription data (nationwide registry of prescribed drugs, health surveillance system for prescribed MPH), 2006	0–18 years	MPH 2006: 2.5%, 10-year-old boys: 7.7%, 10-year-old girls: 2.4%
Vinker et al. 2006, Israel (20)	Regional health insurance data (Clalit HMO), 1998–2004	0–18 years	MPH (2004): 2.5%
Huissoud et al. 2007, Switzerland (14)	Prescription data on Ritalin (methylphenidate) from pharmacies (canton of Vaud), 2002	Under 20 years	Ritalin: 0–19 years: <1%, 5–14 years: 0.74%
Knellwolf et al. 2007, France (21)	Health insurance company billing data for self employed persons, 2003–2005	6–18 years	MPH 2005: 0.18%
Hugtenburg et al. 2004, Netherlands (15)	PHARMO database (drug dispensing data), 2001	0–18 years	Psychoactive drugs: 2.29%, MPH: 1.0%
Asheim H et al. 2007, Norway (16)	Norwegian Prescription Database (NorPD), 1.1.2004–30.6.2004	4–17 years	Stimulants: 4–17 years: 1.1% (6-month prevalence), 10–13 years: boys: 2.4%, girls: 0.8%
Schmidt-Troschke et al. 2004; Germany (22)	Prescription data of a statutory health insurance carrier in the state of Mecklenburg-West Pomerania, 2000–2001	2–25 years	6–10 years: 1.3%, 11–15 years: 1.4%
Janhsen 2006, Germany (8)	Data from the Gmünder Ersatzkasse health insurance carrier, 2006	0–17 years	MPH (2006): 1.7%, boys: 2.7%, girls: 0.7%
Schubert et al. (current study)	Sample of insureds of the statutory health insurance carrier AOK Hesse/KV Hesse, 2006	0–18 years	MPH (2007): 1.1%, boys: 1.7% (95% CI: 1.5–1.88), girls: 0.4% (0.33–0.49)

MPH, methylphenidate; HMO, Health Maintenance Organization

Jugendpsychiatrie], 2007 [2]). In any case, there remains the important question whether, and to what extent, the total recommended daily doses were exceeded (8). It should be pointed out here that multimodal treatment—i.e., treatment with both psychoactive medication and psychotherapy—is held by the guidelines to be essential, but is still inadequately implemented in clinical practice (3, 23). The question whether restricting drug approval criteria improves this situation can and should be investigated by monitoring prevalences, treatments, and prescribing physician groups with the aid of routinely obtained data. Analyses of these types can also yield “yellow flags” of possible relevance to public health policy. The findings of the present study, for example, raise the question whether the increased prescribing of methylphenidate in older age groups might be associated with non-indicated use, e.g., for the

purpose of improving cognitive performance (“neuro-enhancement”). Another possibility is that the spectrum of indications may have been widened to include aggressive and dissocial manifestations; there is some evidence that this is already the case for atypical neuroleptic drugs (24, e4, e5). Moreover, it is clear that the topic of HKD in adulthood requires greater attention (25), and that a solution must be found to the problem of off-label use for correct indications in young adults over age 18.

Conflict of interest statement

The PMV Research Group has received project support from health insurance carriers, private foundations, and the following drug companies: Sanofi-Aventis, Novo-Nordisk, Lilly, Sanofi-Pasteur-MSD, Bayer-Schering, Merz, Janssen-Cilag, and Abbott. Dr. Ingrid Schubert and Ingrid Köster did not receive any personal payments. Professor Gerd Lehmkuhl received research support from Lilly Deutschland GmbH and Bristol-Myers Squibb and serves on the Eli Lilly Straterra Advisory Board.

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ORIGINAL ARTICLE

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A Study of Data From a Random Sample of Insurees of the AOK Health Insurance Company in the German State of Hesse, 2000–2007

Ingrid Schubert, Ingrid Köster, Gerd Lehmkuhl

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