Psychopharmacological Prescriptions in Children and Adolescents in Germany

A Nationwide Analysis of Over 4 Million Statutorily Insured Individuals From 2004 to 2012

Sascha Abbas, Peter Ihle, Jürgen-Bernhard Adler, Susanne Engel, Christian Günster, Roland Linder, Gerd Lehmkuhl, Ingrid Schubert

SUMMARY

Background: In view of the well-known increase in prescriptions of stimulants for children and adolescents over the last 20 years, it is important to study trends in the prevalence and incidence of the use of other psychotropic drugs by this age group as well, to enable an early response to potential problems in the current care situation.

Methods: We used nationwide data from German statutory health insurance funds (Allgemeine Ortskrankenkasse [AOK], all insurers; Techniker Krankenkasse [TK], a 50% randomized sample) concerning all insurees aged 0–17 years (5.0 million people in 2012) to study trends in the prevalence and incidence of psychotropic medication use as well as initially prescribing medical specialties over the period 2004–2012, both for the overall group of psychotropic drugs and for selected subgroups of drugs.

Results: From 2004 to 2012, the prevalence of psychotropic drug prescriptions (not including herbal and homeopathic substances) for children and adolescents rose from 19.6 to 27.1 per 1000 individuals. Marked rises were seen for stimulants (10.5 to 19.1 per 1000) and antipsychotic drugs (2.3 to 3.1 per 1000), while the prevalence of antidepressant prescriptions remained constant at about 2 per 1000. The rates of new prescriptions from 2006 to 2012 were generally constant or decreasing; for the overall group of (non-herbal, non-homeopathic) psychotropic drugs, the rate of new prescriptions fell from 9.9 to 8.7 per 1000. There was a trend toward the issuance of new prescriptions by medical specialists, rather than by family physicians and pediatricians.

Conclusion: The observed increased prevalence of psychotropic drug use among children and adolescents appears to be due not to an increased rate of initial prescriptions for these drugs, but rather to a rise in the number of patients who, once having received such drugs, were given further prescriptions for them in the years that followed.

Cite this as
Methods

The study was based on data from two statutory health insurance companies, the AOK (all children and adolescents insured) and the TK (50% random sample), on all children and adolescents aged 0–17 years between the years 2004 and 2012. In 2012, the final year of observation, the total study population comprised 3.57 million continuously insured children and adolescents in the AOK and 0.72 million in the TK. Since the TK sample comprised 50% of child and adolescent members, TK data were weighted twofold. Thus, the results presented here (N, percentage, per 1000) are representative of the population of all children and adolescents insured by the TK and the AOK.

Prevalences were defined as the percentage of continuously insured children and adolescents with at least one prescription, including infants continuously insured from birth (0 years), in the relevant year. Incidence was measured as the percentage of children and adolescents receiving at least one prescription and no corresponding prescription in the previous 730 days (2 years), taking into account continuously insured individuals in the observation year and two previous years.

The total group of psychotropic drugs, i.e., psycholeptics and psychoanalactics with the anatomical therapeutic chemical [ATC] classifications (22) N05 and N06, was included in the study, excluding active herbal/homeopathic substances (N05BP, N05CP, N05H, N06AH, N06AP). Thus, the focus of the general overview was on allopathic drugs. The following five pharmacological subgroups were analyzed separately according to the ATC system:

- Antipsychotics (N05A)
- Anxiolytics (N05B)
- Hypnotics and sedatives (N05C)
- Antidepressants (N06A)
- Psychostimulants (N06BA).

Only drug prescriptions issued in the outpatient sector were considered in the analysis, including prescriptions issued by institutions authorized to participate in contractual health care, e.g., outpatient units.

Specialist physician groups were identified by physician identifier number according to the medical specialist group code.

Statistical methods (Poisson regression, PROC GENMOD, Statistical Analysis Software [SAS]) were used to calculate whether prescription rates had changed significantly over the years, taking into consideration differences in age and sex structures. The resulting relative risks can be interpreted as percentage changes in the administrative treatment prevalence/incidence over the years.

The significance level was defined as p<0.001. As with prevalence and incidence estimates, Poisson regression was performed with the doubly weighted TK data. However, a comparison of Poisson regression with single and double weighting showed no difference in significance at the level p<0.001. The Microsoft Structured Query Language (MS SQL) Server 2008 and SAS 9.3 were used for descriptive and analytical statistics.

Results

The overall prescription prevalence for psycholeptics/psychoanalactics, excluding herbal/homeopathic preparations, rose from 19.6 in 2004 to 27.1/1000 in 2012; however, it remained largely constant after 2009 (Figure 1a, eTable 1). In contrast, the rate of new prescriptions declined steadily after 2007 (Figure 1a, eTable 2).

The prescription prevalence of stimulants increased from 10.5 in 2004 to 19.4/1000 in 2010, remaining largely constant ever since (Figure 1a, eTable 1). The corresponding new prescription rate declined already as of 2008 (Figure 1a, eTable 2).

The antipsychotic prevalence rate increased from 2.3 in 2004 to 3.1/1000 in 2012 (Figure 1b, eTable 1). In contrast, the corresponding incidence was relatively constant at approximately 1.0–1.1/1000 (Figure 1b, eTable 2). A consideration of the subgroups shows that this rise can be attributed to an increase in atypical antipsychotic drugs (eTable 2).

From 2009 onwards, a slight increase in antidepressant prevalence was observed (1.9 in 2009 and 2.2/1000 in 2012). Incidence remained relatively constant after 2006 at 1.5/1000. This moderately increased prevalence can be attributed to a marked rise in the 14- to 17-year-old age group (4.8 in 2004 to 6.8/1000 in 2012). However, prevalences in the lower age groups declined. Closer scrutiny of the subgroups shows a rise between 2004 and 2012 in the selective serotonin reuptake inhibitor (SSRI) group, but a decline in the non-selective monamine reuptake inhibitor (NSMRI) group (eTables 1 and 2).

Prescription numbers in the hypnotic, sedative, and anxiolytic drug groups declined, in particular the prevalence of hypnotics and sedatives (4.9 in 2004 to 3.2/1000 in 2012) (Figure 1b, eTables 1 and 2).

The trends in psychotropic drug prevalences and incidences for the groups and selected subgroups shown in Figure 1, as well as in the corresponding significance analysis, are described in detail in eTables 1 and 2. The prevalence of antipsychotic drugs and stimulants rose between 2004 and 2012, while the prevalence of hypnotics and sedatives dropped significantly (p<0.001) (eTable 1). In contrast, no significant trend was observed for the prevalence of antidepressants and anxiolytics (p>0.001). Only new prescription rates for stimulants increased significantly, while those for hypnotics and sedatives showed a marked decrease between 2006 and 2012 (eTable 2).

An age and sex specific analysis showed higher new prescription rates for boys in the stimulant and antipsychotic groups (eFigure 1). In the antidepressant group, the highest new prescription rates with an upward trend were seen in 14- to 17-year-old girls (4.7 in 2006 to 6.5/1000 in 2012) (eFigure 1). Stimulant incidences were highest among 7- to 10-year-olds (eFigure 1).

Almost 78% of all new recipients of antidepressants were aged between 14 and 17 years (Figure 2). Those receiving stimulants, in contrast, fell predominantly into the 7- to 10-year-old age group. The benzodiazepine diazepam, as well as first-generation antihistamines
Prevalence and incidence of selected psychotropic drugs per 1000 children and adolescents between 2004 and 2012

a) Psycholeptics/psychoanaleptics (excluding herbal/homeopathic medicines), herbal/homeopathic psycholeptics/psychoanaleptics, stimulants
b) Antipsychotics, anxiolytics, hypnotics and sedatives, antidepressants

Prevalence: solid line, at least one prescription in the relevant year
N: continuously insured individuals in the relevant year:

Incidence: broken line, defined as no relevant prescriptions in the 730 days prior to initial prescription
N: continuously insured individuals in the relevant year and the two previous years:

Herbal and homeopathic medicines were excluded in the psycholeptic/psychoanaleptic group

a) Psycholeptics/psychoanaleptics (excluding herbal/homeopathic medicines), herbal/homeopathic psycholeptics/psychoanaleptics, stimulants
b) Antipsychotics, anxiolytics, hypnotics and sedatives, antidepressants

With a sedative effect (doxylamine and promethazine), account for the high percentage of 0- to 2-year-olds receiving their first psycholeptic/psychoanaleptic prescription.

With regard to the physician groups initially prescribing psychotropic drugs, a temporal trend is seen toward specialist physician groups, i.e., child and adolescent psychiatrists/psychotherapists, adult psychiatrists/psychotherapists, and neurologists, a group for which no further differentiation is possible in the data (Figure 3 for the group receiving stimulants; eFigure 2 a, b, c for the corresponding analysis of new recipients of psycholeptics/psychoanaleptics [excluding herbal/homeopathic medicines], antipsychotic drugs and antidepressants). Correspondingly, a decline was seen in the percentage of pediatricians and general practitioners issuing initial prescriptions. This trend was particularly marked in relation to the initial prescription of stimulants (Figure 3): here, the percentage of child and adolescent psychiatrists/psychotherapists, adult psychiatrists/psychotherapists, and neurologists issuing initial prescriptions rose from 33.8% in 2006 to 43.4% in 2012.

Almost 50% of all new recipients of antipsychotic drugs had received another psychotropic drug in the previous 2 years—a stimulant in 35.7% of cases (Figure 4).
Discussion

This study represents the largest investigation to date into trends in psychotropic drug use in children and adolescents in Germany. The analysis revealed that the prescription prevalences of all psychotropic drugs (excluding herbal/homeopathic medicines), stimulants, and antipsychotic drugs rose between 2004 and 2012, whereas new prescription rates declined or remained constant. The increased prevalences of psychotropic drug use appear to be based less on the number of children and adolescents newly receiving pharmacological treatment than on the fact that more patients that had received treatment in the past went on to receive repeat treatment in the following years. Analyses conducted in other countries (with different study periods, age groups, and data sources) have also revealed a marked rise in the prevalence of treatment with psychotropic drugs overall (10, 11). This is in line with the guideline recommendations stating that antidepressants should not be administered before adolescence. However, here again, further studies are needed to establish whether sufficient non-drug treatment methods are being offered.

The short-term decrease in prescription prevalences between 2004 and 2006 could be interpreted—as also concluded in other studies—as the result of warnings issued by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) of increased suicidality under SSRI treatment (24, 25). Indeed, our data show that the sharp rise in SSRI prescriptions in children and adolescents in Germany reported between 2000 and 2003 (18) stagnated from 2004 to 2006 and only started to rise again in 2006. The data in this analysis reflect not only the rising trend in stimulant prescriptions that has long been described, but also the decline seen in recent years (16, 17). The decrease in new prescription rates for methylphenidate was already observable in 2008. However, the prevalence and incidence of treatment with stimulants rose in Italy, for example (data up to and including 2011) (12). Prevalences also rose in Australia and Slovenia (data up to and including 2012) (14, 26).
In line with the present study, international studies show an increase in psychotropic drug prescriptions, in particular atypical drugs (10–14).

Children receiving a psychotropic drug prescription for the first time had often been previously treated with stimulants. Further analyses show a diagnosis of hyperkinetic disorder in 36% of these recipients (27). The fact that the indication for psychotropic medication was coded as a diagnosis in only a small number of recipients (27) suggests that these drugs are also being used beyond the approved indication (off-label). Bachmann et al. reported similar findings on the basis of the BARMER-GEK data (6).

The increase in specialist physician groups issuing initial prescriptions should be seen in a positive light and may be due, for stimulants at least, to changes in prescription regulations in 2010, among other factors.

This study provides evidence of an increase in the prevalence of psychotropic drugs up to 2009, with levels remaining stable until 2012. A look at trends for other drugs, based on data of the AOK (nationwide) during the same period, revealed a steady increase in the group of pain relief and antipyretic drugs, as well as a steady decline in antibiotic use (28). We can therefore conclude that prescription trends need to be considered in an indication-specific manner.

The reasons for the increase in psychotropic drug use may be manifold. A rise in mental disorders in Germany that could account for an increase in the use of psychotropic drugs was not supported either by a meta-analysis tracking the long-term trend between 1953 and 2007 (2) or by the second wave of the KiGGS study (3, 4). A recent Danish study reported that taking an increase in the use of health care services over time into consideration mitigated rises in psychotropic drug use to a considerable extent (29). The number of physicians active in the field of child and adolescent psychiatry/psychotherapy (+ 53%) and pediatric and adolescent medicine (+ 15%) in Germany actually rose sharply between 2004 and 2012 (30). Moreover, comparative data from 2003 to 2006 and from 2009 to 2012 confirm findings from the KiGGS study that child and adolescent medicine is increasingly used (31). The association between the increased use of psychiatric/psychotherapeutic health care services between 1996 and 2012 and the severity of mental illness was investigated using recent data from the US (11). The authors concluded that the absolute rise is accounted for primarily by children with low-level or no impairment, while children and adolescents with severe mental illness account for the largest relative rise in the use of mental health services (11).

Strengths of the present study include the large size of the database, as well as the fact that it brings together data from two nationwide health insurers catering to different clientele in terms of socio-economic background. This makes the study results more representative compared with results obtained using data from
only one statutory health insurance company (32). Since privately insured children, who tend to have higher socioeconomic status (32) and a known inverse association with increased risk of mental illness (33), were not included in the study, it can be assumed that prescription rates compared with those for all children and adolescents in Germany were slightly overestimated. Furthermore, data were not subject to a selection or recall bias, since all drugs prescribed and subsequently dispensed by a chemist were included in the analysis. However, no data is available on whether the medications were actually taken, which may have resulted in a slight overestimation of prescription rates. In addition, the study was not able to include over the counter (OTC) preparations. As a result, it is possible that a level of underreporting has taken place, particularly in terms of herbal/homeopathic prescriptions, as well as hypnotics and sedatives, in this case the first-generation OTC antihistamines.

The question of whether the rising trend in the prescription of psychotropic drugs in children and adolescents represents an over-provision of health care is currently part of a controversial scientific discussion particularly in the US (34–36), and is also under debate in Germany, primarily with regard to the prescribing of stimulants. The data presented here do not permit conclusions along the lines of “too much.” Nevertheless, a critical discussion on the observed increase in prescriptions is needed within the specialist community—particularly with regard to atypical drugs. The rise in prescriptions also needs to be seen against the backdrop of the long waiting times reported for psychotherapeutic treatment in Germany.

The observed trend toward a decrease in the prescribing of stimulants could be interpreted as physicians’ and parents’ assuming a more cautious stance toward pharmacotherapy as a result of prescribing restrictions, greater attention drawn to guideline recommendations, and possibly not least the critical public debate. This should also encourage the formation of a critical awareness of other substance groups, such as antipsychotic drugs, by means of well-founded guidelines and information. However, the increased use of these drugs also points to significant shortcomings: firstly, the range of treatment offered for children with externalizing disorders is inadequate; and secondly, sufficiently evaluated treatment programs are lacking. However, it is also necessary to ensure that increased stressors in children and adolescents are recognized early on and counteracted through social, educational, or structural interventions. Failure to do so risks spawning the desire to solve social problems with medication.

**FIGURE 4**

Percentage receiving prescriptions for other psychotropic drugs in the 2 years prior to new prescriptions in the group of new recipients of antipsychotic drugs, antidepressants, and stimulants in 2012

The percentage receiving relevant pretreatment in the six selected groups is shown for new recipients of stimulants (gray bars), antidepressants (red bars), and antipsychotics (blue bars). Example: 36% of new recipients of antipsychotics already received stimulants in the 2 previous years. Herbal and homeopathic medicines were excluded in the psycholeptic/psychoanaleptic group.

N (new recipients): antipsychotics = 4628; antidepressants = 6564; stimulants = 15 140
The prevalence of treatment with psychotropic drugs rose between 2004 and 2012. However, differences are visible between the pharmacological groups: although the percentage of children and adolescents using stimulants rose until 2010, the new prescription rate has decreased slightly since 2008. The prevalence of treatment with antipsychotics, in contrast, increased significantly.

Psychotropic drug prescriptions have been increasingly issued by specialist physician groups in recent years, while general practitioners and pediatricians have played a less important role.

Continuous insuree-related monitoring based on routine data from statutory health insurance companies would seem reasonable as a means to promptly identify the prescribing prevalence and practices for psychotropic drugs. This would enable a description of the status quo of treatment under everyday conditions.

A critical discussion on prescribing practices, particularly in relation to antipsychotics, is needed—possibly accompanied by prescribing regulations, as seen with stimulants.

Acknowledgments
The authors wish to thank the scientific advisory board of the study, Dr. Anselm Bönte, Prof. Oliver Frick, Prof. Martin Holtmann, Dr. Monika Panhuysen, and Prof. Holger Pfaff, for their constructive discussion and numerous suggestions.

Funding
The study was funded by the Federal Ministry of Education and Research (grant number: 01GY1130).

Conflict of interest statement
Dr. Abbas received payment for authorship/co-authorship of a publication relating to this subject from Schattauer Verlag, Stuttgart.

Dr. Engel and Prof. Linder are employed by the Scientific Institute of the TK for Benefit and Efficiency in Health Care (Wissenschaftliches Institut der TK für Nutzen und Effizienz im Gesundheitswesen, WINEG).

Dipl.-Soz. Wiss. Adler and Dipl.-Math. Günster are employed by the Scientific Institute of the AOK (Wissenschaftliches Institut der AOK, WIdO).

Prof. Lehmkuhl and Mr. Ihle state that no conflict of interests exists.

Manuscript submitted on 22 October 2015, revised version accepted on 18 February 2016.

Translated from the original German by Christine Schaefer, BA Hons, Postgraduate Diploma in Technical and Specialized Translation.

REFERENCES


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### Trends in prevalence per 1000 children and adolescents for selected psychotropic drugs between 2004 and 2012

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<th>RR2</th>
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**RR1** refers to percentage changes in prevalence per year (RR1) or per 8 years (RR2); prevalence: at least one prescription in the relevant year; herbal and homeopathic medicines were excluded in the psycholeptic/psychoanaleptic group. NSMRI, non-selective monoamine reuptake inhibitors; RR, relative risk; SSRI, selective serotonin reuptake inhibitors.

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**Supplementary material**

**Psychopharmacological Prescriptions in Children and Adolescents in Germany**

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Dtsch Arztebl Int 2016; 113: 396–403. DOI: 10.3238/arztebl.2016.0396

**eTABLE 1**

Trends in prevalence per 1000 children and adolescents for selected psychotropic drugs between 2004 and 2012

<table>
<thead>
<tr>
<th>Year</th>
<th>Psychotropic/psychoanaleptic</th>
<th>RR1</th>
<th>RR2</th>
<th>p</th>
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**RR1** refers to percentage changes in prevalence per year (RR1) or per 8 years (RR2); prevalence: at least one prescription in the relevant year; herbal and homeopathic medicines were excluded in the psycholeptic/psychoanaleptic group. NSMRI, non-selective monoamine reuptake inhibitors; RR, relative risk; SSRI, selective serotonin reuptake inhibitors.
**TABLE 2**

**Trends in incidence per 1000 children and adolescents for selected psychotropic drugs between 2006 and 2012**

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<td>0.3</td>
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<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.94</td>
<td>0.6</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Stimulants</strong></td>
<td>4.5</td>
<td>4.6</td>
<td>4.2</td>
<td>3.9</td>
<td>3.7</td>
<td>3.6</td>
<td>3.7</td>
<td>0.96</td>
<td>0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>– Methylphenidate</td>
<td>4.3</td>
<td>4.6</td>
<td>4.5</td>
<td>4.1</td>
<td>3.9</td>
<td>3.7</td>
<td>3.6</td>
<td>0.97</td>
<td>0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>– Atomoxetine</td>
<td>0.8</td>
<td>0.9</td>
<td>0.9</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.92</td>
<td>0.6</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Herbal/homeopathic psycholeptics/psychoanaleptics</strong></td>
<td>13.8</td>
<td>13.2</td>
<td>13.2</td>
<td>11.8</td>
<td>11.6</td>
<td>9.9</td>
<td>10.0</td>
<td>0.92</td>
<td>0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>– Homeopathic and anthroposophic psycholeptics</td>
<td>12.2</td>
<td>11.7</td>
<td>11.9</td>
<td>10.6</td>
<td>10.5</td>
<td>8.9</td>
<td>8.9</td>
<td>0.92</td>
<td>0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>– St. John’s wort</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.93</td>
<td>0.6</td>
<td>0.002</td>
</tr>
</tbody>
</table>

N (continuously insured individuals in the relevant year and previous 2 years): 2006: 5 018 219; 2007: 4 656 180; 2008: 4 250 002; 2009: 4 122 714; 2010: 4 104 375; 2011: 4 211 358; 2012: 4 239 461; Poisson regression adjusted for age and sex; RR refers to percentage changes in incidence per year (RR1) or per 6 years (RR2); incidence: at least one prescription in the relevant year and no corresponding prescription in the 730 days prior to initial prescription; herbal and homeopathic medicines were excluded in the psycholeptic/psychoanaleptic group. NSMRI, non-selective monoamine reuptake inhibitors; RR, relative risk; SSRI, selective serotonin reuptake inhibitors.
eFIGURE 1 Incidence of selected psychotropic drugs per 1000 children and adolescents between 2006 and 2012 according to age and sex

a) Psycholeptics/psychoanaleptics (excluding herbal/homeopathic medicines)
b) Antipsychotics
c) Antidepressants
d) Stimulants

Boys: solid line
Girls: broken line

Incidence is defined as no corresponding prescription within 730 days of the initial prescription; N (continuously insured individuals in the relevant year and the two previous years):


Herbal and homeopathic medicines were excluded in the psycholeptic/psychoanaleptic group.
eFIGURE 2

Distribution according to physician group issuing the initial prescription (%)

a) Psycholeptic/psychoanaleptics (excluding herbal/homeopathic medicines)
b) Antipsychotics
c) Antidepressants

Herbal and homeopathic medicines were excluded in the psycholeptic/psychoanaleptic group.
Outpatient units could not be given separately and are included in “Other physicians.”

N (new recipients): psycholeptics/psychoanaleptics (excluding herbal/homeopathic medicines) = 35,511; antipsychotics = 4,628; antidepressants = 6,564