

Effectiveness and Cost of Atypical versus Typical Antipsychotic Treatment for Schizophrenia in Routine Care

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Abstract

Background: In two recent randomised clinical trials, a meta-analysis and in an effectiveness study analysing routine data from the U.S. Veterans Administration the superiority of the newer atypical drugs over typical antipsychotic drugs, concerning both their efficacy and their side-effect profile, has been questioned.

Aims of the Study: To analyse the effectiveness and cost of atypical versus typical antipsychotic treatment for schizophrenia in routine care.

Methods: Cohort study using routine care data from a statutory sickness fund with 5.4 million insured in Germany. To be included, patients had to be discharged with a diagnosis of schizophrenia in 2003 and fulfil membership criteria. Main outcome measures were rehospitalisation rates, mean hospital bed days, mean length of stay, cost of inpatient and pharmaceutical care to the sickness fund during follow-up and medication used to treat side-effects.

Results: 3121 patients were included into the study. There were no statistically significant differences in the effectiveness of atypical and typical antipsychotics on rehospitalisation during follow-up (rehospitalisation rate ratio 1.07, 95% confidence interval 0.86 to 1.33). However, there were consistent observations of atypical antipsychotics being more effective for severe cases of schizophrenia (14.6% of study population; >61 prior bed days per year in 2000-2002) in the follow-up period, whereas for the other severity strata typical antipsychotics seemed more effective in

reducing various rehospitalisation outcomes. Patients treated with atypical antipsychotics received significantly less prescriptions for anticholinergics or tiaprid (relative risk 0.26, 95% confidence interval 0.18 to 0.38).

Discussion: The effectiveness of atypical antipsychotics for schizophrenia on rehospitalisation measures appeared similar to that of typical antipsychotics. With the exception of severe cases, the higher costs for atypical antipsychotics were not offset by savings from reduced inpatient care. Major limitations include the lack of statistical power for subgroup analyses, the lack of clinical severity scale data and of life-course medical history data which both increase the risk of residual confounding by disease severity.

Conclusions: This study provides evidence that the effectiveness of atypical and typical antipsychotics measured in terms of hospital readmissions appears to be similar in routine care.

Implications for Health Care Provision and Use: From a clinical perspective, this study provides evidence that the effectiveness of atypical and typical antipsychotics measured in terms of hospital readmissions appears to be similar in routine care.

Implications for Health Policies: Routine data studies can yield valuable information for policy decision-makers on the costs and the effectiveness of pharmaceuticals in routine care, complementing efficacy data from randomised clinical trials currently used for licensing and reimbursement decisions.

Implications for Further Research: The non-significant differences in the effectiveness of atypical compared to typical antipsychotics according to severity of disease should be investigated in a prospective observational study or in a randomised clinical trial.

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Introduction

Schizophrenia is a chronic disease with superimposed exacerbations of psychotic symptoms and a life time prevalence of approximately 0.7%, and an annual incidence of 20-22 cases per 100,000 inhabitants.¹ It affects a broad range of mental and neuropsychological functions including thinking, perception of reality, ideation, concentration and motivation, in addition to hallucinations and delusional beliefs. A third symptom complex is formed by social

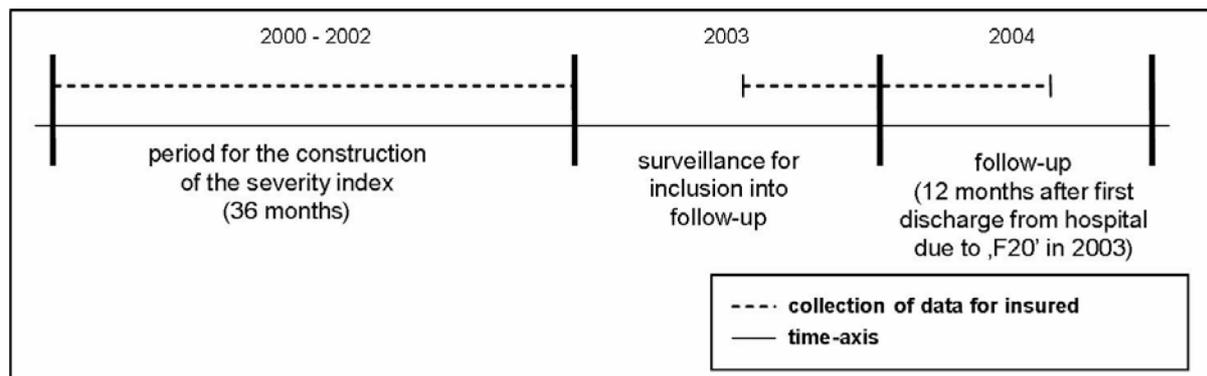


Figure 1. Setting and Data Collection.

isolation, loss of sense of pleasure, an inability to make decisions, and poor self-care.²

The early age of onset of the disease – usually in the twenties often preceded by a long prodromal period – connected with a chronic course, frequent and long hospital stays and temporary or permanent inability to work makes the disease very costly.^{1,3} In the Global Burden of Disease Study, schizophrenia ranks at the fifth place accounting for 1.15% of the total burden of disease measured in disability-adjusted life years (DALYs) in western Europe.⁴ At least one third of patients with schizophrenia develop a chronic course of illness. Because every episode of schizophrenia worsens lifetime prognosis, prevention of relapse is one of the major therapeutic goals.⁵

Since the first market launch of atypical antipsychotics in the 1970s, the superiority of the newer atypical drugs over typical antipsychotic drugs, concerning both their efficacy and their side-effect profile, has been repeatedly demonstrated.^{6,7} However, these claims have been questioned in recent randomised clinical trials (RCT),⁸⁻¹⁰ a meta-analysis,¹¹ and in an effectiveness study analysing routine data from the U.S. Veterans Administration.¹² A key concern in the debate about the differential efficacy and effectiveness of atypical compared to typical antipsychotics has been the substantially higher cost of atypical drugs. Based on limited data from one RCT¹³ it has been claimed that these could be offset by the higher efficacy of the newer drugs to reduce rehospitalisation, leading to cost savings for inpatient care.¹⁴ We therefore compared the effectiveness and cost of atypical versus typical antipsychotics in a real-world setting using routine data from the Techniker Krankenkasse, a German sickness fund with more than 5.4 million insured. The study therefore also demonstrates how administrative data can be used to compare the effectiveness of drugs under real world conditions.

Methods

Setting and Design

Improving therapy adherence is a major therapeutic goal in schizophrenia, as relapse – which in turn often results in

rehospitalisation – is thought to worsen long-term prognosis. Improved compliance because of more acceptable medication may thus improve long-term outcomes.¹⁵ Consequently mean hospital bed days and rehospitalisation rates during follow-up were chosen as the main outcome parameters for this study. In previous effectiveness studies, readmission to hospital or days in hospital have been used in a similar way.¹⁶⁻¹⁹ Cost of inpatient care, cost of antipsychotic treatment and cost for other pharmaceuticals were assessed from a public payer perspective.

To compare the effectiveness of atypical and typical antipsychotics, routine data including prescriptions and the number of days in hospital with a diagnosis of schizophrenia (ICD-10, F20.0 to F20.9) were collected from the Techniker Krankenkasse (TK), a German sickness fund (public health insurer) with more than 5.4 million insured (i.e. 8% of German residents with public health insurance) which operates nationwide and competes with other sickness funds for customers. Members of the TK from all German federal states with a hospitalisation due to a diagnosis of schizophrenia were followed up for 12 months after their first discharge from hospital in 2003. To control for possible bias or confounding by severity of disease, data on prior hospitalisations with a diagnosis of schizophrenia was collected for 2000, 2001 and 2002 (see **Figure 1**). Data on psychopathological scales are not recorded in German sickness fund databases.

Cohort

In 2003, 3397 TK insured were hospitalised at least once with schizophrenia. A total of 5604 hospital episodes were reported. 164 patients were excluded because membership in the sickness fund ended during follow-up. Another 112 insured were excluded, because membership in the sickness fund during the period used to construct the severity index was less than 365 days. The final study population comprised 3121 patients with a mean age of 37.1 years (range 12 to 84 years). 1760 patients (56.4%) were male, 1361 (43.6%) were female.

Outcome Measurement

Outcome data on rehospitalisation of each patient was collected during follow-up (rehospitalisation rate, hospital bed days with a diagnosis of schizophrenia per year, number of hospitalisations per year). In addition, the cost of treatment to the sickness fund and the number of prescriptions for medications commonly used to treat side-effects of antipsychotics were collected. These included prescriptions for anticholinergics and the neuroleptic tiaprid to treat extrapyramidal symptoms, anxiolytics to treat anxiety, and prescriptions for hypnotic and sedative drugs to treat insomnia or agitation.

Exposure Measurement

To determine exposure, prescription data for antipsychotics were collected for each patient for 12 months after the beginning of the individual follow-up period. Prescription data contained all drugs dispensed to the patient. Outpatient medication was identified by ATC-code and by prescribing date. The 3121 patients were classified into seven different groups according to the antipsychotic drug treatment received in the outpatient sector. A patient was considered to be treated with an 'atypical' antipsychotic if she/he received amisulpride, clozapine, olanzapine, quetiapine, risperidone, ziprasidone or zotepine. Within this group we differentiated between patients always receiving the same antipsychotic during follow-up ('non-switchers') and different antipsychotics ('switchers').

The typical antipsychotic drugs were divided into a group of high potency typical antipsychotics (benperidol, bromperidol, flupentixol, fluphenazine, fluspirilene, haloperidol, perazine, perphenazine, pimozid, thioridazine, zuclopenthixol) and a group of low potency typical antipsychotics (chlorpromazine, chlorprothixene, levomepromazine, melperone, pipamperone, promazine, promethazine, prothipendyl, sulphirid). If a patient received typical antipsychotics only, he was referred to be treated with a 'typical' antipsychotic. Again, a differentiation between switchers and non-switchers was made.

Patients receiving both atypical and high potency typical antipsychotics were categorized as 'atypical and typical'. Patients who received atypical drugs and low-potency typical antipsychotics were labelled 'atypical with adjuvant therapy', as the low-potency medication is often added for its sedative effect. The remaining patients who did not receive prescriptions for antipsychotics in the outpatient sector were classified as being treated 'without medication in the outpatient sector'.

According to sickness fund prescription data, 1372 patients (43.9%) were treated with atypical antipsychotics only and 499 patients (16.0%) were treated in addition with a low potency typical antipsychotic. 327 patients (10.5%) were treated with a typical antipsychotic only. 645 patients (20.7%) were treated with high potency typical and atypical antipsychotics. The remaining 278 patients (8.9%) had no prescription record for medication in the outpatient sector.

Stratification by Severity of Disease

A severity index was constructed dividing the number of days in hospital with an ICD-10 diagnosis of F20.X in 2000, 2001 and 2002 by days of membership with the sickness fund. The ratio was multiplied by 365 resulting in a severity index expressed as mean prior days hospitalised per year. 2778 patients (89.0%) were members of the Techniker Krankenkasse during the whole period for the construction of the severity index (three years), while the remaining 343 (11.0%) had at least one year of membership.

A case was referred to be a 'new' case if the patient had not been hospitalised in 2000, 2001 and 2002. In total, there were 1301 new cases (41.7%) among the study population. However, this group not only includes newly diagnosed cases, but also cases belonging to other severity strata as the period for the construction of the severity index is between one and three years for each patient, so some patients may have been hospitalised before the observation period. The remaining patients were classified as mild cases of schizophrenia (first quartile of severity index; 0-14 days in hospital per year, n=453), moderate cases of schizophrenia (second and third quartiles of severity index; 14-61 days in hospital per year, n=912) and severe cases of schizophrenia (fourth quartile of severity index; more than 61 days in hospital per year, n=455). The study population classified by medication and severity grade is presented in **Table 1**.

Statistical Analysis

Statistical analyses were conducted using SAS version 9.1. The study had the statistical power to detect a 10% risk difference in rehospitalisation rates between patients treated with atypical and typical antipsychotics, assuming an equal proportion of patients treated with either type of drug. As the mean number of bed days during follow-up was not normally distributed, the Wilcoxon-Mann-Whitney U test (SAS npar1way procedure) was used to test for statistical significance of differences. Cost differences between groups were tested using the Student t-test. A P-value of less than 0.05 was considered to indicate statistical significance.

Results

Rehospitalisation Rates

During follow-up, 1598 patients (51.2% of the study population) were hospitalised at least once, which is comparable to hospitalisation rates in another routine data study.²⁰ The average number of hospitalisations during follow-up was 1.06 (range 0 to 23) per year. The average length of hospitalisation was 38.6 days (range 1 to 364).

Readmission rates were 47.7% for patients treated with atypical antipsychotics, 44.6% for patients treated with typical antipsychotics, 56.3% for those treated with atypicals with adjuvant therapy, and 63.7% for patients treated with atypical and high potency typical drugs. For patients without

Table 1. Study Population (N = 3121) by Medication and Severity Grade.*

Medication	Severity Grade				
	New case (0)	Mild (0-14)	Moderate (14-61)	Severe (>61)	All severity grades
Atypical					
Atypical (non-switchers)	472	148	299	117	1036
Atypical (switchers)	130	50	106	50	336
Atypical with adjuvant therapy	199	68	155	77	499
Typical					
Typical (non-switchers)	78	29	48	19	174
Typical (switchers)	48	23	53	29	153
Atypical and typical	213	101	201	130	645
Without medication in outpatient sector	161	34	50	33	278
All medication groups	1301	453	912	455	3121

* Severity Grades: Mean Days of Prior Hospitalisation Per Year.

Table 2. Mean Days Hospitalised with a Diagnosis of Schizophrenia during Follow-Up (standard deviation) by Medication and Severity Grade.

Medication	Severity Grade							
	New case		Mild		Moderate		Severe	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Atypical								
Non-switcher	23.1	(45.2)	26.2	(50.9)	31.4	(50.2)	48.6	(70.4)
Switcher	49.0	(66.1)	44.7	(57.3)	48.0	(59.3)	57.4	(66.1)
Atypical with adjuvant therapy	31.8	(46.2)	23.8	(42.5)	39.8	(58.7)	75.0	(73.5)
Typical								
Non-switcher	16.4	(40.7)	12.1	(24.2)	21.2	(37.1)	82.1	(95.4)
Switcher	19.8	(37.0)	16.2	(26.1)	30.5	(39.4)	37.5	(41.7)
Atypical and typical	35.4	(52.9)	37.1	(51.4)	51.3	(62.6)	71.8	(76.3)
Without medication in outpatient sector	15.5	(45.0)	20.3	(35.4)	35.6	(52.2)	69.0	(97.5)

medication in the outpatient sector, the readmission rate was 38.1%. The rehospitalisation rate ratio as a measure of relative risk for patients treated with atypical antipsychotics only, compared to those treated with typical drugs only was 1.07 (95% confidence interval 0.86 to 1.33). However, when patients were stratified according to disease severity, consistent differences in the effectiveness of the two types of antipsychotics were observed, which are detailed in the following analyses.

Mean Number of Bed Days during Follow-up

For new, mild and moderate severity cases of schizophrenia, the mean days of hospitalisation during the follow-up period were lower if they received typical compared to atypical antipsychotics (non-switchers: 16.4 days vs. 23.1 days for new cases [$p=0.1459$], 12.1 days vs. 26.2 days for mild cases

[$p=0.5039$] and 21.2 days vs. 31.4 days for moderate cases of schizophrenia [$p=0.0913$]). However, the mean bed days for severe cases were lower if treated with atypical antipsychotics (non-switchers: 82.1 days vs. 48.6 days [$p=0.1052$]). For complete results see **Table 2**.

The differences in the mean bed days during follow-up can be either attributed to variations in the average length of stay, to variations in the average number of readmissions during follow-up or both. For new and mild cases of schizophrenia, the average length of stay and the average number of stays was lower if patients were treated with typical antipsychotics compared to patients being treated with atypical antipsychotics. For moderate cases of schizophrenia the difference in the mean bed days between typical and atypical antipsychotic treatments was mainly due to a reduction of average number of readmissions, while there was almost no difference in average length of stay for the two drug classes.

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Table 3. Differences in Mean Days Hospitalised, Average Length of Stay and Average Number of Stays during Follow-Up Stratified by Severity of Schizophrenia

Medication	Severity Grade			
	New case	Mild	Moderate	Severe
Mean days hospitalised				
Atypical (non-switcher)	23.1	26.2	31.4	48.6
Typical (non-switcher)	16.4	12.1	21.2	82.1
Difference	6.7	14.1	10.2	-33.5
Two-sided Wilcoxon text for significance of differences in means	atyp <> typ p=0.0909	atyp <> typ p=0.3872	atyp <> typ p=0.1685	atyp <> typ p=0.1228
Average length of stay (if hospitalised)				
Atypical (non-switcher)	40.0	39.9	37.1	47.2
Typical (non-switcher)	34.6	21.9	37.7	44.1
Difference	5.4	18.0	-0.6	3.1
Two-sided Wilcoxon text for significance of differences in means	atyp <> typ p=0.1919	atyp <> typ p=0.0730	atyp <> typ p=0.7289	atyp <> typ p=0.8173
Average number of stays				
Atypical (non-switcher)	0.62	0.70	0.98	1.21
Typical (non-switcher)	0.46	0.59	0.58	2.00
Difference	0.16	0.11	0.40	-0.79
Two-sided Wilcoxon text for significance of differences in means	atyp <> typ p=0.1267	atyp <> typ p=0.5581	atyp <> typ p=0.1119	atyp <> typ p=0.1200

For severe cases of schizophrenia with a prior hospitalisation of more than 61 days a year, the difference in mean bed days (33.5 days) in favour of atypical antipsychotics was due to a reduced number of hospital readmissions during follow-up (1.21 vs. 2.00), although the average length of stay was slightly higher if treated with atypical antipsychotics (47.2 days vs. 44.1 days). Differences in all three outcome measures (mean days hospitalised, average length of stay, average number of stays) were not significant between patients treated with typical antipsychotics compared to patients treated with atypical antipsychotics (see **Table 3**).

Controlling for other Possible Confounders

Results were standardised by age using the direct method of standardisation. The distribution of the whole study population was taken as the standard population and 5 different age groups (<25; 25-35; 35-45; 45-55; >55 years) were defined. An additional standardisation by gender was not conducted as it would have required splitting medication/severity/age groups into 360 subgroups. Standardisation by age reduced differences in outcomes between the two drug classes in favour of atypical antipsychotics, although the results did not change significantly (see **Figure 2**).

In addition, the use of depot drugs was analysed. Although the percentage of patients having received at least one antipsychotic depot medication in the typical group (26.6%) was substantially higher than in the atypical group (1.8%), the number of patients in each subgroup receiving depot drugs only was too low to further subdivide the groups. In total 48 patients were exclusively treated with typical

antipsychotic depot drugs and 18 patients exclusively with atypical depot drugs. Compared to oral antipsychotics, depot drug use reduced rehospitalisation rates (relative risk 0.78; 95% confidence interval 0.5 to 1.24) and mean hospital bed days during follow-up (26.6 vs. 34.7 bed days). However, because of the small sample sizes the difference in mean hospital bed days during follow-up was not significant. 957 patients (30.7% of the study population) were prescribed antidepressants during follow-up, 189 patients (6.1%) were prescribed anticonvulsants and 124 patients (4.0%) received both. Prescription of antidepressants or anticonvulsants did not confound the results.

Cost of Treatment

Average total cost of treatment for patients belonging to the two non-switcher medication groups was € 6254. Average inpatient expenditure amounted to € 4810 for both groups. In accordance with the results for mean number of bed days, treatment with atypical antipsychotics (non-switchers) led to higher inpatient expenditure than treatment with typical drugs (non-switchers) for new, mild and moderate cases of schizophrenia (new cases: € 3602 vs. € 2191 [p=0.1330], mild cases: € 4820 vs. € 4519 [p=0.8746], moderate cases: € 5517 vs. € 3641 [p=0.1669]), while it led to lower inpatient expenditure for severe cases of schizophrenia (€7509 vs. € 12158 [p=0.1773]). Total expenditure on pharmaceuticals and inpatient care was higher if patients were treated with atypical drugs for new [p=0.0137], mild [p=0.3845] and moderate cases [p=0.0235] compared to those treated with typical antipsychotics, while total

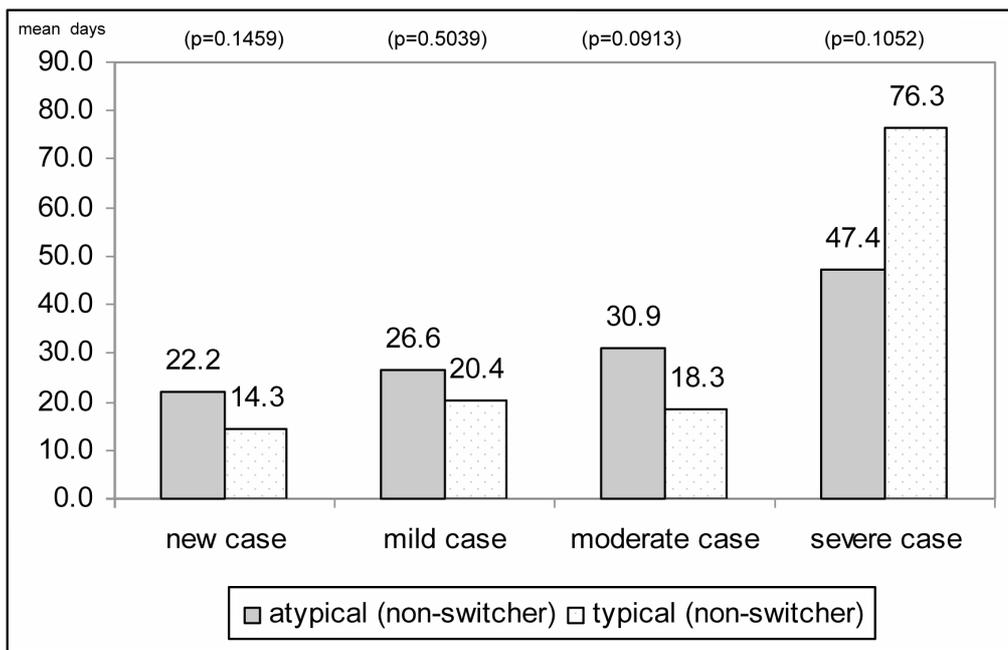


Figure 2. Mean Hospital Bed Days with a Diagnosis of Schizophrenia during Follow-Up (Standardised By Age).

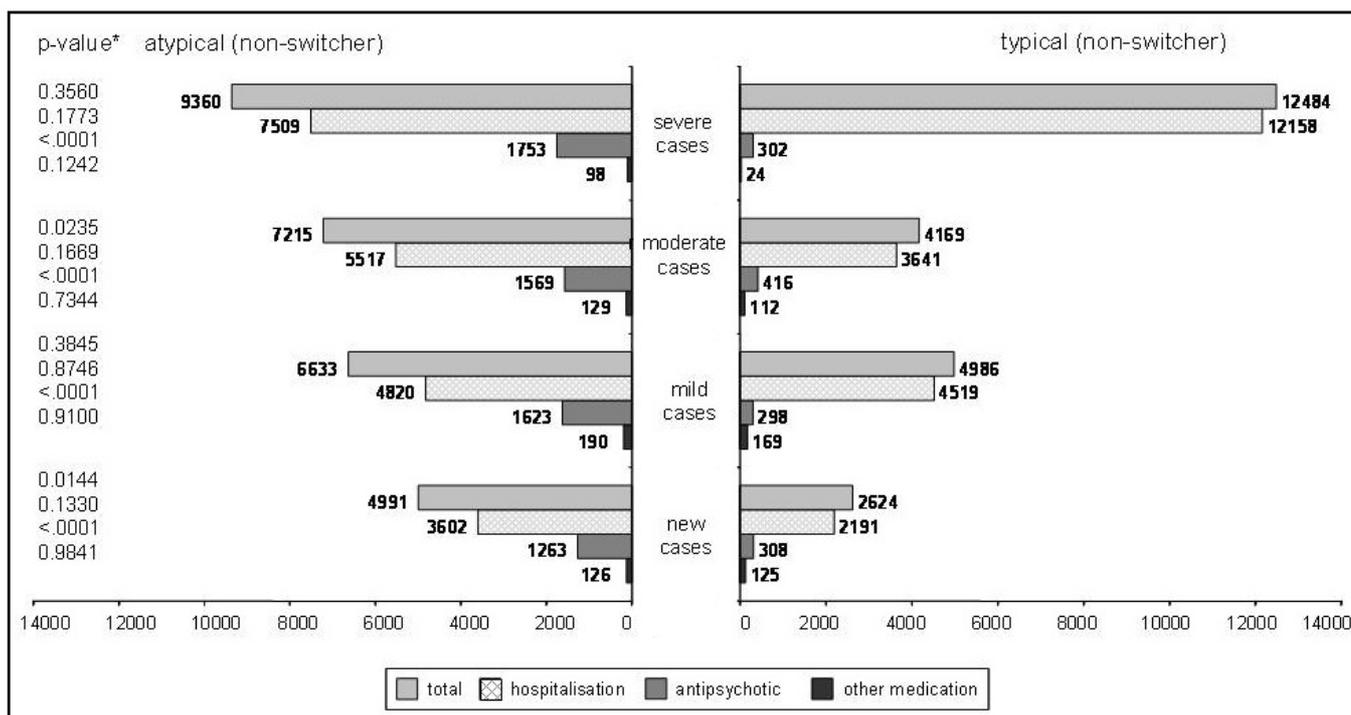


Figure 3. Costs of Inpatient and Pharmaceutical Care (adjusted by age).

Note: * two sided t-test

expenditure was lower for severe cases of schizophrenia [p=0.3560] (see **Figure 3**).

Side Effects

Only 7.8% of patients treated with atypical antipsychotics (non-switchers) received prescriptions for anticholinergics or tiaprid compared to 30.5% of patients receiving typical

antipsychotics (relative risk 0.26, 95% CI 0.18 to 0.38). Patients on atypical antipsychotics also received less prescriptions for hypnotic and sedative medications (RR 0.66; 95% CI 0.43 to 1.02) and less prescriptions for anxiolytics (RR 0.83, 95% CI 0.56 to 1.24) when compared to typical drugs. However, the differences in the latter two groups of psychopharmacological medications were mainly due to differences in patients' age, as after standardising

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results for age only the difference in prescriptions for anticholinergics or tiaprid persisted.

Discussion

In this 'real world' retrospective cohort study of patients with schizophrenia, the effectiveness of atypical antipsychotics on rehospitalisation measures appeared not significantly different to that of typical antipsychotics. There was a significant difference concerning prescriptions for anticholinergics or tiaprid, commonly used to treat extrapyramidal symptoms, in favour of atypical antipsychotics. However, as these medications might have also been prescribed as prophylactic treatment, our proxy measure for side effects might be biased. Although the observed differences did not reach statistical significance, there were observations that atypical drugs might be more effective for severe cases of schizophrenia, and typical drugs for new, mild and moderate cases. With the exception of severe cases, the higher costs for atypical antipsychotics were not offset by savings from reduced inpatient care.

These findings are important as they support findings from randomised clinical trials,^{8,9} a meta-analysis,¹¹ and a real-world effectiveness study,¹² which did not find significant differences in efficacy or effectiveness between atypical and typical antipsychotics. In the present study, the effectiveness of the two types of drugs seems largely to depend on the severity of schizophrenia as measured by previous hospitalisations. We observed a non-significant trend towards higher effectiveness of atypical antipsychotics in reducing rehospitalisation for severe cases, but not for new, mild, and moderate cases, although these results did not reach statistical significance. The similar effectiveness and higher cost of atypical medication thus has to be balanced with the more favourable side effect profile concerning movement disorders of atypical drugs shown in the results of numerous RCTs and meta-analyses.^{6,11}

The results for the 'no medication in the outpatient sector' group are difficult to interpret. At first glance they seem counterintuitive: it is generally assumed that patients who discontinue their antipsychotic medication after a hospitalisation should do worse than compliant patients. However, this has never been studied in a real world setting and maybe a longer follow-up is needed to detect the effect of immediate discontinuation of treatment on rehospitalisation. Some of the patients, especially those that have been classified as new cases, might also have been misdiagnosed or miscoded patients with schizoaffective disorder. In addition, our study did not have the statistical power to test this hypothesis at the sub-group level and therefore the observed lower rehospitalisation rate may be due to chance.

The design of the study – a cohort study using routine data – allowed us to analyse a substantial study population with complete datasets concerning their hospitalisations and prescriptions. Nevertheless, the use of administrative data limits the generalisability of the results.^{21,22} In contrast to randomised clinical trials or prospective observational

studies, neither data from clinical severity assessments were available nor information on other factors known to influence the risk of relapse such as engagement in community services, living conditions or family background.^{23,24} Utilization of outpatient care or non-physician care, e.g. psychoeducation, could not be examined. Furthermore, it is well-known that psychopathology or hospital readmission rates only partially reflect general outcome. Quality of life, psychosocial re-integration, and the occupational situation are other important factors to measure effectiveness.

The low number of patients treated only with typical antipsychotics (10.5%) was unexpected as it does not correspond to the overall prescription pattern of antipsychotics for all indications in Germany for 2003 (69% prescriptions for typical and 31% for atypical antipsychotics, in WHO defined daily doses).²⁵ The unequal sizes of our exposed populations obviously reduced the statistical power of this study. The high number of "new" cases in our study population is probably due to the fact that the period for the construction of the severity index was limited to the three years preceding the index hospitalisation as the datasets before this timepoint were incomplete. Thus, this severity stratum not only includes newly diagnosed cases, but also some patients with more distant prior hospitalisations.

Available data did not allow us to differentiate to what extent hospital readmissions were due to medication response or to non-compliance. According to Weiden and Olfson the loss of efficacy of antipsychotics after one year is caused by loss of medication response in 68% and due to non-compliance in 32% of cases.²⁰ Atypical antipsychotics seem to achieve higher compliance rates than typical drugs.^{7,26,27} However, we could not assess to what extent wrong dosage strength or non-compliance contributed to hospital readmission in our study. Another limitation is that all atypical antipsychotics were considered as a homogenous group of drugs. In reality, there are differences in the efficacy and particularly in the side-effect profile between individual atypical drugs.^{9,19,28}

In addition, prior hospitalisation is only one measure for the severity of schizophrenia and it is unknown to what extent it corresponds to psychopathological rating scales used to determine severity in the clinical setting. Prior hospitalisation itself may have been influenced by the type of neuroleptic treatment or switching behaviour during the previous three or more years. Potential bias also arises from the thresholds constructed to differentiate different severity strata as they are based on statistical quartiles. However, even if the severity strata constructed in this study do not correspond to clinical severity scales, it will be important to control for prior hospitalisations in future effectiveness and efficacy studies. Controlling for the severity of schizophrenia can also partially explain differences in reported outcomes of previous studies. For example, the study conducted by Essock *et al.*¹⁸ showing a superior efficacy of clozapine compared to typical antipsychotics, included only patients who had been hospitalised at least during two of the preceding five years.^{18,29} The findings for these patients with an average of at least 144 days prior hospitalisation per year

match our findings for severe cases of schizophrenia (> 61 prior bed days per year and an average prior hospitalisation of 101.9 days per year within the group). In the study by Rosenheck *et al.*⁸ which found no significant difference in the efficacy of olanzapine compared to haloperidol, the average hospitalisation in the preceding year was presented in intervals only. Assuming a uniform distribution within the intervals, the average prior hospitalisation in the Rosenheck *et al.* study population would be 37.0 days per year, which is comparable to the second and the third quartile of our severity index (prior hospitalisation between 14 and 61 days per year), for which we did not observe significant differences in effectiveness between the two types of antipsychotic medication neither.

Conclusions

This study provides evidence that the effectiveness of atypical and typical antipsychotics measured in hospital readmissions appears to be similar in routine care. The increased cost of atypical drugs is not offset by cost-savings in inpatient care. Thus, the claims of earlier randomised trials that atypical antipsychotics are superior to typical drugs with respect to hospital readmissions does not apply to routine care. From a clinical perspective, the lack of significant differences in the effectiveness of atypical compared to typical antipsychotics in routine care is the most interesting finding of our study and confirms more recent randomised clinical trials. We raise the hypothesis that both classes of antipsychotics vary in their effectiveness depending on the severity of disease. This research question should be investigated in a prospective observational study or in a randomised clinical trial. Although rehospitalisation might be the most important outcome parameter from an economic perspective,³⁰ atypical antipsychotics with their more favourable side-effect profile concerning movement disorders might still be the preferred treatment option from the doctor's and the patient's perspectives. However, recently two cost-effectiveness studies based on utility measurements found no significant difference in quality of life between patients treated with atypical antipsychotics compared to patients treated with typical antipsychotics.^{31,32}

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