

# Psychiatric Decision Making in the Adoption of a New Antipsychotic in Germany

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**Objective:** Studies in somatic medicine have demonstrated delays in the implementation of new drugs, but data on psychiatric drugs are scarce. This study examined psychiatrists' adoption of a new antipsychotic. **Methods:** A prospective survey of 50 hospital psychiatrists in Germany was conducted three months before and three months after the market introduction of aripiprazole. Psychiatrists' awareness and perceptions of the drug and psychiatrist-related data were obtained before the launching of aripiprazole; actual prescription patterns were recorded afterward. **Results:** Predictors of major concerns about the credibility of statements related to efficacy or tolerability of the drug were older age and longer work experience of the psychiatrists. Three months after market introduction, 79 percent of the psychiatrists had already prescribed the new antipsychotic. Predictors for early adoption were older age, being responsible for patients with mild mental illness, and having a higher tolerance of uncertainty. **Conclusions:** Despite concerns as to the credibility of statements about aripiprazole's efficacy and tolerability, the psychiatrists were found to be early adopters of the new compound. The predictors identified for early adoption show the importance of physician-related factors for the quality of everyday care. (*Psychiatric Services* 57:700–703, 2006)

Studies from other medical fields have demonstrated a long delay in the implementation of new research findings or in the use of new drugs, leading to suboptimal treatment of patients (1). However, the early uptake of unnecessary or ineffective new therapies is criticized as causing a financial burden on health systems.

It has been shown that individual physicians differ strongly as to how they adopt new strategies and how rapidly they implement them. The speed at which the physicians take up innovative new drugs depends not only on drug characteristics but also

on physician characteristics (2–4).

From a political viewpoint, the challenge is to promote the uptake of innovations that have been shown to be effective, to delay the spread of those that have not yet been shown to be effective, and to prevent the uptake of ineffective innovations (1).

In mental health there is currently a heated discussion about the use of the second-generation antipsychotics. On the one hand, their widespread use is urgently advocated for and supported by data that suggest advantages relating not only to fewer extrapyramidal side effects but also to

improvements in, for example, negative symptoms, cognitive functioning, and subjective well-being (5,6). On the other hand, these advantages are challenged by findings that tend to support therapeutic equivalence of the cheaper first-generation antipsychotics (7–9).

Information on how psychiatrists adopt new drugs and which factors influence their decisions is scarce, because research in the field of medical decision making has made only limited inroads into psychiatry (10). It was thus our aim to perform an explorative study of psychiatrists' adoption of a new drug.

## Methods

Three months before and three months after the launch of the antipsychotic agent aripiprazole (Abilify) in June 2004, we conducted semi-structured interviews with 50 hospital psychiatrists in Southern Germany. Aripiprazole was chosen as the drug to be studied because it was the next antipsychotic to be introduced on the German market and because it was announced as a “third-generation” antipsychotic, with a new mechanism of action, partial dopamine agonism. To recruit psychiatrists, we contacted five psychiatric hospitals: one university hospital and four state hospitals. The survey was introduced to the psychiatrists at morning rounds as a study about antipsychotic drug choice (without naming aripiprazole), and psychiatrists currently treating pa-

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tients with schizophrenia were included in the survey.

The first interviews were undertaken in March or April 2004. Aripiprazole was launched in June 2004, and the second interviews were conducted in September 2004.

In conducting the interviews we were interested in the following topics. Which sources of information do the psychiatrists use in general? The frequency of use of different sources of information was measured by 5-point rating scales. Possible scores range from 1, never, to 5, regularly. Are the psychiatrists aware of the forthcoming introduction of the new drug? ("Have you heard or read about a drug called aripiprazole, or Abilify, prior to this interview?") Where did they learn about the new product? ("On which occasion did you first hear about the new drug?") How do they perceive statements on aripiprazole's efficacy, tolerability, and mechanism of action (as stated by the manufacturer)? Are the statements credible? How important are the stated efficacy, tolerability, and mechanism of action to their clinical work? Which patients do they intend to give this agent to, and which patients do they not? (From their currently treated patients, psychiatrists were requested to provide sociodemographic data, information on current medication, and scores on the Clinical Global Impression scale for the patients most likely and least likely to be given aripiprazole.) How many psychiatrists used the new agent three months after introduction? What variables influenced these patterns?

Additionally, sociodemographic information about the psychiatrists was obtained, and the psychiatrists filled in a questionnaire, Ungewissheitstoleranzskala (UGTS), which assessed their uncertainty tolerance (11). The UGTS is an 8-item self-report questionnaire devised to measure a person's assessment of ambiguous situations. The UGTS showed satisfactory internal consistency ( $\alpha=.72$ ). It has been shown that individuals can be distinguished according to their tolerance of uncertainty. Previous research has demonstrated that patients with a high uncertainty tolerance are more likely to search for new health-related information (11). However,

this measure has not been used in the context of psychiatrists' decision making. We hypothesized that psychiatrists with a high uncertainty tolerance would be more likely to adopt the new drug within the first three months after its introduction.

We performed an exploratory analysis of the data. Frequency statistics, nonparametric tests, and linear regression analysis were applied. A  $p$  value of  $<.05$  was considered significant.

## Results

Fifty psychiatrists from five psychiatric hospitals participated in the survey; 47 were surveyed at follow-up. Thirty-nine (78 percent) were men, and 11 (22 percent) were women. Thirty-three (66 percent) were residents, 16 (32 percent) were senior psychiatrists, and one (2 percent) was the department head. Their mean  $\pm$  SD age was  $41.6 \pm 7.1$  years, and their mean term of experience was  $10.1 \pm 7.8$  years. Forty (80 percent) were working with inpatients, five (10 percent) were working with outpatients, and five (10 percent) were working with both inpatients and outpatients.

Among the most frequently used sources of information (mean scores of 3 or greater) were journals, colleagues, morning rounds, congresses, textbooks, the Internet, and contacts with representatives of the pharmaceutical industry. The psychiatrists seldom used advertisements, the hospital's pharmacy, brochures from the pharmaceutical industry, or vocational training (mean score of less than 3).

All but one of the psychiatrists were aware of the new antipsychotic agent due to be introduced to the German market in three months. Ten (20 percent) of them had already had experiences with the drug from participating in clinical trials carried out for registration purposes. The first contact with the new product was at congresses (seven psychiatrists, or 14 percent) or through colleagues (five psychiatrists, or 10 percent), drug company representatives (13 psychiatrists, or 26 percent), the phase III study (14 psychiatrists, or 28 percent), journals (seven psychiatrists, or 14 percent), or in-house training (six psychiatrists, or 12 percent). Other forms of contact occurred through a patient (one psychia-

trist, or 2 percent), the Internet (one psychiatrist, or 2 percent), or pharmacy (one psychiatrist, or 2 percent).

The psychiatrists were shown statements that documented the attributes of aripiprazole, which were derived from clinical trials. The statements are shown in Table 1 and were provided by the manufacturer of aripiprazole upon request. All attributes concerning efficacy and side effects were rated as being important for clinical practice (Table 1). However, when asked how reliable these statements were, psychiatrists gave significantly lower ratings (Table 1). The attributes related to the mechanism of action were rated as less important for clinical practice. Here no consistent difference between perceived importance and credibility was found.

Forty-one psychiatrists (82 percent) planned to use the compound immediately upon market introduction.

A linear regression model that used psychiatrists' age, work experience, experience with aripiprazole within clinical trials, uncertainty tolerance, and number of voluntarily treated patients under supervision was applied to predict whether a psychiatrist attributed high or low credibility to the statements. Therefore, a sum score of all credibility items was derived for each category (efficacy, side effects, and mechanism of action) and served as a dependent variable. Cronbach's  $\alpha$  was .89 for the statements on efficacy, .90 for those on side effects, and .90 for those on mechanism of action.

In regard to efficacy and side effects, the age and experience of the psychiatrists predicted the extent to which they believed the attributes presented would hold true; older psychiatrists ( $p=.02$  for efficacy and  $p=.002$  for side effects) and more experienced psychiatrists ( $p=.01$  and  $p=.003$ , respectively) were more skeptical ( $R^2=.17$  and  $.28$  percent, respectively). No such relationship was found for the items on mechanism of action.

The patients for whom aripiprazole was considered suitable were younger (Mann-Whitney,  $Z=-2.59$ ,  $p=.01$ ), had a shorter duration of illness (Mann-Whitney,  $Z=-2.56$ ,  $p=.01$ ), and had fewer previous hospitalizations (Mann-Whitney,  $Z=-2.93$ ,  $p=.003$ ). The patients not likely to have

**Table 1**

Survey responses of 50 psychiatrists in Germany about the importance and credibility of statements about aripiprazole

Statement	Importance <sup>a</sup>		Credibility <sup>b</sup>		Z	p
	Mean	SD	Mean	SD		
<b>Efficacy</b>						
Efficacious against positive symptoms	4.6	1.0	3.2	1.1	-4.7	<.001
Efficacious against negative symptoms	4.4	1.0	3.1	1.2	-4.7	<.001
As efficacious as risperidone	3.5	1.3	2.6	1.4	-3.4	.001
As efficacious as olanzapine	3.7	1.2	2.7	1.3	-3.7	<.001
Efficacious within 1 week	4.1	1.1	2.8	1.3	-4.5	<.001
Improves cognitive functions	4.3	.8	2.8	1.2	-5.2	<.001
Efficacious against depressive symptoms	3.7	1.0	2.8	1.2	-4.0	<.001
Efficacious in maintenance therapy	4.7	.6	2.7	1.4	-5.8	<.001
As efficacious as haloperidol	3.6	1.4	2.3	1.4	-4.3	<.001
<b>Side effects</b>						
No more extrapyramidal side effects than placebo	4.5	.9	2.6	1.3	-5.3	<.001
No more weight gain than placebo	4.3	.8	2.7	1.4	-5.5	<.001
No more QT-prolongation than placebo	4.0	1.0	2.9	1.5	-3.9	<.001
No more sedation than placebo	3.6	1.0	3.0	1.4	-2.5	.012
No more prolactin elevation than placebo	3.9	.8	3.0	1.4	-3.1	.002
No more orthostatic problems than placebo	4.0	.7	2.9	1.5	-3.8	<.001
<b>Mechanism of action</b>						
Stabilizes the dopamine-serotonin system	3.2	1.2	3.6	1.3	-1.9	.057
Partial D2 agonism	3.3	1.2	3.8	1.3	-2.0	.041
Stabilizes the dopamine system	3.1	1.3	3.2	1.3	-.3	.790
Stabilizes the serotonin system	3.0	1.3	3.0	1.4	-.1	.886
Partial antagonism at 5HT-1A	3.0	1.3	3.3	1.5	-1.9	.063
Antagonism at 5HT-2A	3.1	1.3	3.4	1.6	-1.5	.125

<sup>a</sup> Psychiatrists were asked, "How important would it be for your daily work if the following statements would hold true?" Possible responses ranged from 1, not important, to 5, very important.

<sup>b</sup> Psychiatrists were asked, "How credible are these statement in your view?" Possible responses ranged from 1, not credible, to 5, very credible.

aripiprazole prescribed were more often prescribed first-generation antipsychotics ( $\chi^2=10.5$ ,  $df=2$ ,  $p=.005$ ). No further differences were found between the two groups.

Three months after the introduction of aripiprazole, 37 of 47 psychiatrists had already prescribed the drug (79 percent).

A logistic regression model that used several variables—psychiatrist's age, work experience, experience with aripiprazole, uncertainty tolerance, and number of voluntarily treated patients under his or her supervision—was applied to predict whether a psychiatrist would adopt the new drug within the first three months. The model predicted 43 percent of the variance ( $R^2=.43$ ). Older psychiatrists ( $p=.033$ ), those treating more patients on a voluntary basis ( $p=.022$ ), and those expressing higher uncertainty tolerance ( $p=.045$ ) were more likely to have prescribed aripiprazole within three months after its launching.

## Discussion

No delay in the adoption of aripiprazole by the psychiatrists was found. Reasons for this finding might be because psychiatrists were well informed and because some of them had already had experiences with the drug before the market introduction. Most of them had their first contact with aripiprazole through phase III studies or drug company representatives. Thus, in the case of aripiprazole, the information on the drug had been disseminated very effectively. Hence aripiprazole might fall into that category of new drugs in which public demand boosts implementation (3).

It can be viewed as positive that psychiatrists were well informed before prescribing a new compound and were willing to adopt innovations at an early stage. However, the influence of the manufacturers might conceivably lead to biased information and unfavorable influence on psychiatrists' decision making. In the case of

aripiprazole, the market introduction had been postponed several times because registration was delayed, with the marketing having already started before the launch.

Some skepticism on the psychiatrists' part was found in the discrepancy between the perceived importance of certain drug characteristics and the credibility of the description. Apparently psychiatrists had a desire for an effective drug without side effects but doubted whether aripiprazole would fulfill these expectations. Experiences with previous market introductions may have played an important role here. One might even suggest that the more market introductions a psychiatrist has witnessed, the more skeptical he or she becomes toward marketing strategies. However, this skepticism, adequately expressed in our interviews, had no influence on the psychiatrists' prescription of the new drug. On the contrary, psychiatrists who expressed the greatest concerns (the older psychiatrists)

were more likely to be early adopters of the drug.

This finding not only appears paradoxical but also contradicts earlier findings of our research group that showed that older physicians were more likely to prescribe older drugs (12). One explanation for this discrepancy might be that in the study presented here, we interviewed only hospital psychiatrists (who are less autonomous in their habits), whereas in the previous study, we also studied psychiatrists in private practice. Not only did psychiatrists' age predict the early adoption of the drug, but their working environment and their personality characteristics also affected whether they adopted the drug within three months after launch. Thus psychiatrists who worked with patients undergoing treatment voluntarily were more likely to adopt the drug early. This finding goes hand in hand with the finding that the perceived "ideal" patient for aripiprazole tends to be mildly ill and under treatment with second-generation antipsychotics, whereas the patients with more critical illness (treated on an involuntary basis) might still be prescribed well-known, first-generation drugs. This behavior might reflect skepticism as to the efficacy of the new compound or a strategy of cautious action.

If the latter is the case, the dissemination of new drugs would be expected to begin with the patients with mild illness and proceed to those with more severe mental illness. This strategy is of interest, because an opposite one could also be imagined (treating nonresponders with a drug having a new mechanism of action).

From a review of these results it might be concluded that we have found a perfect example of rapid implementation of an innovative drug. However, neither we nor the psychiatrists studied know whether aripiprazole will really prove to be an effective and tolerable agent that is superior to its comparators (see the discussion of second-generation antipsychotics in studies by Rosenheck and colleagues [8] and Lieberman and colleagues [9]). This question can be answered only after intensive use of the agent under naturalistic condi-

tions and examination in randomized controlled trials.

More important in our view, however, are the observed variations in the psychiatrists' prescribing behavior that are based on the psychiatrists' characteristics—age, working environment, or uncertainty tolerance. In view of the recent debates about whether second-generation antipsychotics really have advantages over first-generation antipsychotics or whether selective serotonin reuptake inhibitors are used too frequently, it seems vital to obtain a deeper insight into how psychiatrists adopt new drugs and how information or education about new therapies should best be disseminated.

Because this was an exploratory study, statistical statements are to be seen as generating rather than confirming hypotheses. It is at least possible that our presentation of information on aripiprazole during the first interviews might to some extent have worked as an intervention. On the other hand, it is a strength of the survey that it was undertaken prospectively (before the introduction of the compound) and that we conducted a follow-up survey with the same psychiatrists after the launch of the drug.

## Conclusions

Hospital psychiatrists were shown to be early adopters of a new antipsychotic compound. This finding might be due to the fact that the psychiatrists were confronted even before market introduction with a wealth of information on the drug, mainly from the manufacturer. Despite their expressed skepticism about the drug's claims, most psychiatrists had no inhibitions about prescribing the new drug within three months after market introduction. It is not clear whether the psychiatrists adopted an important innovation at an early stage, thereby giving the best treatment available to their patients, or whether their prescribing practice was disadvantageously influenced by marketing strategies and a more cautious adoption of the new drug would be desirable. Finally, the impact of practice variation requires further evaluation.

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