Patients' perspectives. Subjective experiences and attitudes of patients with recent onset schizophrenia

de Haan, L.

Citation for published version (APA):
de Haan, L. (2002). Patients' perspectives. Subjective experiences and attitudes of patients with recent onset schizophrenia

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)

Download date: 19 Dec 2018
General discussion
The studies of attitudes and subjective experiences of patients described in this thesis follow on earlier research into symptoms, family aspects, family intervention, personality factors and biological traits of patients with recent-onset schizophrenic disorders carried out in the Adolescent Clinic of the AMC/de Meren.

This chapter consists of three parts: 1. Background of the research questions. 2. Observations on the methods used. 3. Implications for treatment and research and relationship to other findings.

1. Background of the research questions

The interactive phenomena that constitute so much of human experience cannot be understood properly if they are viewed merely as representatives of brain functions. Ideas and convictions can only be comprehended in a social context. Neural or cognitive psychological processes can never fully explain the vulnerability to, or the manifestation, course and treatment of psychiatric disorders. A convincing explanation will have to integrate higher psychosocial levels of explanation with more basal levels. This means that knowledge of interpersonal interaction as well as of the meaning and motivation underlying behavior is needed to arrive at a comprehensive explanatory model (Henningsen and Kirmayer, 2000). Although all mental processes are associated with events in the brain, it is a simplification to conclude that all mental processes are determined by the brain and that all mental disorders are essentially disturbances in brain function. The psychosocial process that we call mind comes about through the interplay of brain, body and environment, and it is impossible to explain this interplay if we limit ourselves to the intrapersonal or intracerebral level (Oyama, 2000). This also applies to psychiatric disorders and their interpretation. Psychosocial explanations and interpretations are largely dependent on the context, which means that generalization is difficult, but they must remain part of the explanatory framework of psychiatry. Psychological explanations do have to be in agreement with the more basal levels of neurological science. The interpretation of effects of psychotherapy and treatment with medication also becomes more complete if the different levels of explanation are taken into account. At the basal level psychotherapy changes neural networks and gene expression. But that is not all: psychotherapy influences cognition, relations with others and social position. Treatment with psychopharmacologic drugs also has an effect on the personal and cultural significance of a patient's disorder. It changes the attribution and attitude of patients and others with regard to the disorder (Henningsen and Kirmayer, 2000).

The research described in this thesis focuses on the ideas, attitudes and experiences of patients. The research questions arose out of the perspective of
the treatment of patients with psychotic disorders. The underlying idea of this study is that knowledge of the ideas, attitudes and experiences of patients is necessary in order to arrive at successful cooperation and treatment. Psychiatrists ask about the experiences, ideas and views of their patients (thinking, perceiving, feeling, willing). Psychiatrists use what they perceive in order to arrive at a judgment about a psychiatric disorder of a patient. Findings from physical examinations and supplementary diagnostic data are needed to come to a diagnostic decision. But most of the information on which the formulation of the problem and the evaluation of policy are based consists of the experiences, ideas and views of the patient as perceived by the psychiatrist. In other words, the perception of reported information about subjective experiences is the most important method for obtaining information in psychiatry.

This method is problematic because the perception of experiences, ideas and views is always imperfect. This is due to the limitations in the self-revelation by patients but also to the unavoidable interpretation of that self-revelation by psychiatrists. There is, however, no other method better suited for investigating and approaching the nature and severity of psychiatric problems than conversation between patient and diagnostician. In order to limit as much as possible the variability inherent in this method, psychiatrists confer about their perceptions and try to reach agreement about the perception itself, the interpretation of symptoms and diagnostic criteria. Psychopathological measuring instruments and diagnostic classification systems are a consequence of this striving for agreement and reliability.

The subjective character of information collecting in psychiatry has far-reaching ramifications for the degree to which psychiatrists feel certain about their evaluation. Not very long ago a great deal was written about subjective experiences in psychiatric journals. The above-mentioned problems relating to validity and reliability in assessing subjective experiences and the rise of research into biological aspects of mental disorders led to the virtual disappearance of descriptions of subjective experiences from the psychiatric literature. Some even consider the subjective collecting of information a necessary evil. Individual ideas, views and experiences of patients that are not directly related to diagnostics or evaluation of psychiatric policy receive less attention and quickly recede to the background in research and in clinical work. Yet it is necessary to understand the patient’s subjective experience in order to initiate and maintain cooperation. The studies combined in this thesis deal with patients’ ideas, their subjective experiences and their views regarding the mental disorder and its treatment. Knowledge of the individual ideas of patients about their disorder and treatment is extremely important for getting treatment underway and keeping it on track. In evaluating the results of the treatment, the experience of patients once again plays a role. It often happens that patients and those providing treatment differ considerably in their evaluation of treatment results. If patients indicate that they no longer suffer from certain symptoms
targeted by the treatment, the psychiatrist concludes that the treatment has been successful and should be continued. Patients regularly arrive at a completely different conclusion based on their experiences. While it is true that certain symptoms have disappeared, they fell less well: flattened in their emotions, lacking initiative, fatigued or unable to concentrate. It is also possible that they miss certain aspects of the disappeared symptoms or that they now experience symptoms that did not trouble them before. The patient comes to the conclusion that the treatment is not providing the desired effect or that the disadvantages are too great and that the treatment should be changed or stopped.

In patients who are psychotic the above-mentioned factors play a more important role than in non-psychotic patients. The ideas and experiences of patients with a psychosis by definition diverge widely from those of psychiatrists. Their views about the presence of a disorder and the need for treatment often differ as well. This discrepancy in insight is probably related to the speed with which the treatment begins and the way in which it is maintained. There is often a long delay in treatment, and patients who are psychotic are frequently treated involuntarily. After treatment has started approximately only half of the patients with a psychotic disorder persevere in the prescribed treatment. A late start with treatment means that the psychotic symptoms remain present for a longer time, and this has consequences for the functioning of patients in that period as well as for the people who are directly involved with them. In recent years indications have been found that delay in treatment may even have an unfavorable effect on the course of the disorder in the longer term. In addition, stopping the use of antipsychotic medication is the most important cause of the reappearance or exacerbation of a psychosis. Knowledge of the experiences, opinions and ideas of patients therefore has great clinical relevance.

Attention to the experiences and ideas of patients is also necessary in connection with the low self-esteem of many patients. The manifestation of psychotic symptoms brings about a sharp drop in the social hierarchy. Patients suffering from psychotic symptoms notice that they are taken less seriously. This is painful and can lead to avoidance of contact and to a damaged sense of self. For many patients, accepting psychiatric care feels like a capitulation: “I am deranged.” If there is inadequate explicit attention for the ideas, experiences and opinions of patients, their feeling of not being taken seriously will very likely be strengthened.

The last part of this thesis describes research into the occurrence of obsessive-compulsive symptoms in patients with a psychotic disorder. Obsessive-compulsive symptoms can precede psychotic symptoms, develop in the presence of psychotic symptoms, or continue or develop after the disappearance of psychotic symptoms. In some cases obsessive-compulsive symptoms make their first appearance during treatment, and they may then be caused by the treatment with antipsychotic medication.
The debate about a dimensional versus a categorical diagnostic approach is also relevant for the research described here. The prevailing classification system of psychiatric disorders (DSM-IV) does not do justice to the simultaneous occurrence of symptoms belonging to different diagnostic categories. Owing to the hierarchy in the classification system, symptoms that occur in addition to so-called primary symptoms receive less attention, and this may be part of the reason why they are not adequately treated. Dimensional diagnostics offers possibilities to pay closer attention to the diversity of symptoms confronting many patients with schizophrenia.

2. Observations on the methods used

Subjective experience has to be converted into a verbal or non-verbal message in order to be understood by others. Others understand a message of this kind in a unique way. A wide variety of formulations and interpretations of the message are possible. The difficulties that can be associated with this are known as communication problems. Assessing subjective experience is never a simple matter. The reliability of the articulation of subjective experience is uncertain, and worse, the validity of the interpretation of the message about subjective experience is uncertain. Reason enough to avoid the topic of subjective experience in a scientific study. Yet subjective experience is relevant. Clinical psychiatric work is based on knowledge about the subjective experience of patients. Scientific research should support and augment this clinical experience. Research into the relation between subjective experience and other factors can only be conducted if there is a way to measure subjective experience.

In order to assess the ideas of patients regarding their disorder and treatment, patients were asked a number of open questions. The information obtained was subsequently divided into certain categories. This entailed a loss of unique individual information. The advantage, however, was that the results of the study can be summarized in a limited number of categories and that the relation between these categories and other aspects can be investigated.

In order to determine preferences for certain aspects of the treatment, respondents were presented with a list of statements that they were asked to evaluate. The respondents were given no opportunity to indicate unique individual ideas. The instrument does offer the possibility to quantify preferences. The lists with statements about aspects of the treatment were developed after extensive consultation with groups of patients. Individual ideas of patients who were involved in the development of these lists therefore come to expression in the measuring instruments.

In this thesis the concept “subjective experiences of patients during the use of
antipsychotic medication” is defined as follows: all the changes experienced by the patient, both positive and negative, on the physical, emotional and cognitive level, related to treatment with antipsychotic medication. Two problems arise here. How can subjective experience be assessed? How can certainty be achieved about the relation between subjective experience and the use of antipsychotic medication?

The measuring of subjective experience is made possible by having patients evaluate a verbal expression related to their inner life. Here patients had to limit themselves to a fixed list of statements concerning experiences. This method has the disadvantage that unique individual formulations of subjective experience cannot be recorded. The advantage of the method chosen is that a reflection of the experience of patients can be measured, so that the degree to which patients have certain experiences can be followed in the course of time and/or compared between patients. To measure subjective experience we used both a list to be filled in by the patients and a structured interview, because prior to the study we did not know for sure whether patients in a psychotic state would be able to fill in the list themselves in a reliable way.

Regarding the relation between subjective experience and use of antipsychotic medication the following should be noted. It is important to have patients assess subjective experiences without letting them know that a relation is being sought with the use of antipsychotic medication. If patients are aware of the fact that the clinician or researcher is looking for a link between subjective experiences and the use of antipsychotic medication, the articulation of subjective experiences of patients during use of antipsychotic medication will probably be influenced by their ideas about medication. Moreover, it is unlikely that patients and clinicians are able to distinguish subjective experiences related to use of antipsychotic medication from those related to other aspects of the treatment or to the disorder itself. What should be studied is the relation between “blindly” assessed subjective experience and the use of antipsychotic medication. This could be done, for example, by changing the use of antipsychotic medication and then investigating whether this is associated with a change in subjective experience. The above-mentioned method for determining the relation between subjective experience and the use of antipsychotic medication is especially important if one wants to investigate whether there are differences in subjective experience associated with different antipsychotic medications. For research focused on the relation between subjective experience and therapy compliance in clinical practice it is less important to make a distinction between attitude and subjective experience.
Obsessive-compulsive symptoms were assessed with an instrument developed for non-psychotic patients. The distinction between obsessive-compulsive symptoms and psychotic symptoms is problematic. We opted to ascertain obsessive-compulsive symptoms only if a clear distinction could be made in terms of content between psychotic symptoms and obsessive-compulsive symptoms. We did, for example, identify obsessive-compulsive symptoms in a young man who repeatedly had to check whether he had locked the door to his house properly and whether he had asked a question correctly and who in addition suffered from acoustic hallucinations in which strangers commented on his own thoughts. In a young man who repeatedly checked to see whether anyone had entered his room in his absence and who in addition had the psychotic conviction that others were following him or were out to get him we did not identify obsessive-compulsive symptoms because the obsessive actions were related to his psychotic ideas. By identifying symptoms as obsessive-compulsive only if they differ in content from psychotic symptoms, one can avoid finding obsessive-compulsive symptoms in the majority of psychotic patients. The repetitive, intrusive character of many psychotic symptoms would otherwise lead to a frequent identification of obsessive-compulsive symptoms in psychotic patients.

Another criterion used to differentiate psychotic from obsessive-compulsive symptoms is the degree to which patients are aware that the obsessive thoughts, impulses or ideas are a product of their own mind. Some authors (Fenton and McGlashan 1986) suggest that this criterion should not be used to differentiate between psychotic and obsessive-compulsive symptoms in patients with schizophrenia. Although obsessive-compulsive symptoms accompanied by a temporary lack of insight do occur in obsessive compulsive disorder, we identified obsessive-compulsive symptoms in the study described here only if patients had insight into the exaggerated or unwarranted character of the symptoms and ascribed them to their own mental functioning.

The methods in the studies brought together in this thesis are not always ideal. Many questions regarding clinical problems can only be answered by a controlled experiment. This research method is often not applicable. Because, for example, it is not ethical to withhold a certain treatment from patients for a given period of time. Or because the knowledge about long-term effects will only be available far in the future and tentative answers are needed now. For some questions no experiment is necessary, but information should preferably be collected in a prospective study. But this type of study is not always possible or available either. It is not feasible, for example, to investigate the ideas of a group of patients at the moment they become psychotic for the first time. And it is virtually impossible to determine the duration of the untreated psychosis in a prospective way. The application of less ideal methods results in less certainty about the answers found.
3. Implications for treatment and research and relationship to other findings

The confrontation with psychotic symptoms often has dramatic consequences for patients. Most of the patients who suffer from psychotic symptoms come into contact with psychiatric care after some time. For many of them this is also a devastating experience. Usually the ideas patients have about the problems they are experiencing do not agree with the views of family members or professional caregivers. What is more, prior to their psychotic episode patients become acquainted with the ideas prevalent in society about people with mental disorders. Patients will therefore tend to reject psychiatric treatment. Treatment can only be started, however, when there are first signs of cooperation. It is necessary for caregivers to thoroughly acquaint themselves with the ideas of patients. Only if the patient has the impression that his ideas are taken seriously can he meet the caregiver halfway.

Part I

The study of the ideas of patients concerning their first psychotic episode and their treatment has yielded a number of implications for clinical practice. Patients, for example, appear to have widely varied ideas about their disorder and the treatment. There is evidently a complex relation between these ideas and the speed with which treatment comes about.

Starting treatment at the moment when patients themselves realize the need to be treated usually entails a long delay. Achieving cooperation requires of caregivers different, and at times contradictory qualities: patience, perseverance, thoroughness, empathy, respect and modesty.

Patients later emphasize their resistance to accepting treatment. This indicates that great caution is advised. The mere supposition that there could be a link between the duration of untreated psychosis and the prognosis could induce guilt feelings in patients.

When starting a treatment it is important to know the priorities of patients and their family members with respect to the treatment. The study of the priorities of patients and family members relating to the treatment of the first psychotic episode has yielded the following clinically relevant information.

Patients and family members have a need for information about specific problems they are experiencing. Priority should be given to informing them about the disorder and the treatment and helping them deal with the disorder.

Changes in the care offered are desired. Patients attach special importance to outpatient care in their own environment. They also give priority to accessible and safe possibilities for hospitalization.

Patients consider individual consultations to be very important.
Part II
There is a great need for interventions that improve the outcome of schizophrenia. An early start with treatment is promising in this respect. If proof could be found that shortening the duration of untreated psychosis gives a clinically relevant improvement, it would be a major breakthrough. This explains the many studies on this topic recently undertaken and described. There are also clinicians who have already started programs to shorten the duration of untreated psychosis. Yet the question arises whether these dynamic clinical initiatives are supported by the research results presently available.

Beginning treatment as soon as possible after the manifestation of psychotic symptoms can have a favorable effect in the short term. That in itself is reason enough to initiate treatment as quickly as possible. Whether treatment programs aimed at shortening the duration of untreated psychosis also result in improvement in the longer term is unknown. There are indications that especially a duration of untreated psychosis longer than one year is associated with a worse outcome. In the Netherlands the duration of untreated psychosis is usually shorter than one year. (It should be noted here that the long average duration of untreated psychosis reported in studies from other countries is often caused by a few patients with an extremely long duration of untreated psychosis.)

We found no link between the duration of untreated psychosis and aspects of the long-term course in a group of mainly male patients whose family belonged to an association for family members of patients with schizophrenia. Research results presently available do not allow for a definitive conclusion about the extent to which the duration of untreated psychosis is related to outcome (Ho and Andreasen 2001). It remains questionable whether early intervention programs in first-episode patients with a short duration of untreated psychosis can offer the prospect of altering the course of schizophrenia without a sustained comprehensive treatment program (Linszen et al. 2001). This underscores the importance of further research before specific intervention programs aimed at shortening the duration of untreated psychosis are implemented as regular health care. On the other hand many clinician feel the need for a treatment that is started swiftly and maintained over a long period of time, in view of the serious course of schizophrenia in the first years.

In order to answer the question of whether shortening the duration of untreated psychosis improves the prognosis, study has to be made of the long-term outcome of comparable groups of patients who start with treatment at an earlier versus a later point after the development of psychotic symptoms. Studies of the relation between the duration of untreated psychosis and outcome, should be controlling for prognostic factors that cannot be influenced (diagnosis, premorbid functioning, severity of negative symptoms, age at manifestation of psychotic symptoms, sex, rapidity with which psychotic symptoms developed). The relation we found between delay in intensive psychosocial intervention and outcome indicates that the concept of treatment delay should not be limited to delay in treatment with antipsychotic medication but should also include delay...
in psychosocial intervention. A rapid start with intensive psychosocial intervention aimed at the patient and the family could lead to a better course in the short term. Randomized and controlled research is necessary to investigate whether this indication can be confirmed. There are, however, important ethical objections to research of this kind. For this reason it is advisable to first investigate whether the relation mentioned above is found again in another exploratory study.

**Part III**

Antipsychotic medication plays an important role in the treatment of psychoses. Psychotic symptoms can recede to the background under the influence of treatment with antipsychotic medication. If the antipsychotic medication is discontinued the disorder resumes its natural course. In other words, antipsychotic medication does not function as a cure. Antipsychotic medication does not exclusively affect psychotic symptoms but can influence other mental processes as well. In order to suppress psychotic symptoms antipsychotic medication has to affect (inhibit) dopamine neurotransmission. There are two major dopaminergic systems, the extrapyramidal system (projection of dopaminergic neurons from the substantia nigra to the striatum) and the limbic system (projection from the ventral tegmentum to the nucleus accumbens, cortex, amygdala and hippocampus). These systems are involved in the physiological basis of the emotional properties of impressions, experiences and motor activities. Dopaminergic neurotransmission plays an important role in the reward system, and inhibition of this system can be accompanied by reduced motivation, drive and spontaneity. A lower level of dopamine transmission is related to a lesser function of the activations and reward system (Blum et al. 1996). Recently the following findings have been published about characteristics of dopamine transmission and their relation to symptoms and subjective experience of healthy persons and patients. A reduced presynaptic dopamine function was found in the left nucleus caudatus of depressive patients with flattened affect and psychomotoric retardation (Martinot et al. 2001). Reduced availability of D₂ receptors in the putamen and the nucleus caudatus is related to motoric as well as cognitive disturbances in healthy persons (Volkow et al. 1998). Dopamine transporter reduction is related to slower motoric skills and memory defects in detoxified methamphetamine abusers (Volkow et al. 2001). D₂ receptor antagonists have shown a decrease in the subjective ratings of pleasant sensations induced by cocaine (Sherer 1989, Berger 1996). Nicotine stimulates the release of dopamine and the energy metabolism in the basal ganglia, especially in the ventral tegmental areas and the nucleus accumbens (Pontieri et al. 1996), putamen and nucleus caudatus (Salokangas et al. 2000), and this is probably the central reinforcing mechanism of addictive substances (Koob 1992). Cannabinoids also increase the activity of dopaminergic neurons in the ventral tegmentum and the mesolimbic projections; this is accompanied by the desired subjective effects and reinforces the use (Ameri, 1999). A smaller quantity of D₂ receptors predicts a pleasant subjective response to
psychostimulants in healthy persons (Volkow et al. 1999). The frequent smoking of patients with schizophrenia can be understood as a form of self-medication to reduce negative symptoms (Dalack et al. 1998). (In addition smoking reduces the blood level of antipsychotic medication (Goff et al. 1992) and could in this way also affect the inhibiting function of antipsychotic medication that the patient experiences as unpleasant.). A link was found between avoidant personality traits and reduced dopamine \(D_2\) receptor density, particularly in the putamen (Farde et al. 1997, Breier et al. 1998), and dopamine transporter density (Laakso et al. 2000). A relation was also found between low \(D_2\) receptor binding capacity and social phobia (Schneier et al. 2000). In view of the above-mentioned findings, it is highly probable that antipsychotic medication (which inhibits dopamine transmission) influences the subjective experiences of patients. Perceptions and ideas can become less meaningful for them. This is also the desired effect of antipsychotic medication, namely to reduce the significance of hyperindividual false beliefs (delusions) and perceptions (hallucinations). Treatment with antipsychotic medication can, however, also reduce a desirable sense of significance. This is a major problem, considering that reduced drive, motivation, spontaneity and sense of significance also occur inherently in schizophrenia. Treatment with the antipsychotic medication available should inhibit the neurotransmission of dopamine while avoiding too much inhibition. Because treatment with antipsychotic medication very likely affects the subjective experiences of patients, evaluation of these experiences is desirable in order to determine whether some adjustment in the antipsychotic medication is needed. In other words, subjective experience is an important outcome measure in clinical antipsychotic medication research.

Our study has shown that a questionnaire filled in by patients (SWN) can be used to determine the effect of various antipsychotic medications and various doses on the subjective experiences of patients. With this instrument it is possible to investigate whether the type and/or dose of antipsychotic medication affects the subjective experiences of patients. In future research we will also investigate to what extent there is a relation between ideas about antipsychotic medication and subjective experiences during use of antipsychotic medication. The question at issue will be whether it is mainly the opinion about medication or mainly the experience with medication that influences therapy compliance. If negative subjective experience is closely related to the ideas patients have about medication, than it need to be studied whether experiences shape the ideas or the other way around. If the latter is correct, it is less likely that therapy compliance will improve by changing the antipsychotic medication or dosage. In that case improvement of therapy compliance could better be expected from an intervention aimed at changing the ideas patients have about medication than from a change in medication.

In our research we found tentative indications that high \(D_2\) receptor occupancy is related to subjective feelings of non-well-being and to depression as measured by researchers. This relation can be understood as a
validation of the concept "Subjective experience of patients during the use of antipsychotic medication." Our findings agree with those of Bressan et al. (2001), who also found a relation between depression and the degree of D₂ receptor occupancy by antipsychotic medication. Longitudinal controlled research should investigate whether there is a causal relation between increased D₂ receptor occupancy and negative subjective experience. The relation between the degree of occupancy of D₂ receptors by antipsychotic medication and negative subjective experience can be understood as an argument for treatment with antipsychotic medication in doses that avoid an overly high occupancy of dopamine D₂ receptors. We also found preliminary evidence that optimal subjective experience of patients with recent onset schizophrenia is related to D₂ receptor occupancy between 60% and 70%.

There are also various other arguments for treatment with low doses of D₂ antagonists (De Haan and Maksmovic, 1999). Bollini et al. (1994) found in a meta-analysis involving 1638 patients that doses below 2 to 3 mg haloperidol equivalents a day are associated with less effect on positive symptoms. Doses above 7 mg per day are not associated with greater effect, but they are accompanied by more side effects. McEvoy et al. (1991) also found that patients do not improve more if they receive a higher dose than the one at which they develop minimal extrapyramidal side-effects (known as the "neuroleptic threshold dose" Haase, 1961). With higher doses there is an increase in extrapyramidal side effects and negative symptoms. Stone et al. (1995) found no difference in clinical improvement between the group of patients that received 4 mg of haloperidol per day compared with the group that received 10 mg of haloperidol per day. Marder et al. (1987) and Hogarty et al. (1988) found that the psychotic relapse percentage over 2 years in the group with an especially low dose of fluphenazine decanoate (approximately 5 mg/2 weeks) was little higher than in a group that received a standard dose (25 mg/2 weeks). The group with the low maintenance dose had fewer negative and depressive symptoms and a better social functioning. Research on binding has shown that 60% to 74% occupancy of D₂ receptors is optimal for therapeutic effect (Kapur et al. 1996). This occupancy is already reached in first-episode patients with 2 mg of haloperidol per day. To conclude, raising doses above 7 mg haloperidol or an equivalent per day is not associated with more improvement of psychotic symptoms, in most cases, but is associated with more side effects. Particularly for patients with a first psychotic episode low doses (between 2 and 4 mg per day) are important. Similar advice appears applicable to new antipsychotic medications with a strong D₂ antagonism. Since we found substantial interindividual variation in D₂ receptor occupancy at fixed low-dose haloperidol (2.5 mg/day), haloperidol needs to be individualy titrated in the very low dose range to reach optimal occupancy. In addition it is advisable to compare the side effects profile of new antipsychotic medications with that of low doses of selective D₂ antagonists.

However, other factors besides the side effects of antipsychotic medication influence the subjectively experienced quality of life. A recent study (Ritsner et
al. 2001) found that only 3.2% of the variance of subjectively experienced quality of life is determined by side effects of antipsychotic medication, as opposed to 10.1% by difficulties relating to clinical symptoms and 20.9% by psychosocial support.

**Part IV**

We found tentative indications that obsessive-compulsive symptoms are related to the use of certain antipsychotic medications. A confirmation of this relation can be clinically relevant and could clarify pathophysiological mechanisms involved in the development of obsessive-compulsive symptoms. For this reason it would be desirable to conduct prospective controlled studies of the relation between obsessive-compulsive symptoms and clozapine or olanzapine. If the finding mentioned above is confirmed in future research, the clinician should be alert to the development or exacerbation of obsessive-compulsive symptoms during treatment with clozapine or olanzapine. Development or exacerbation of obsessive-compulsive symptoms during treatment with clozapine or olanzapine could have an effect on therapy compliance. It is still unclear whether the addition of antidepressant drugs to the treatment with clozapine and olanzapine helps reduce obsessive-compulsive symptoms. Double-blind randomized controlled studies should be conducted of the treatment of obsessive-compulsive symptoms in schizophrenia patients with antidepressant drugs added to the antipsychotic medication.