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Medication Adherence Decisions in Patients With Schizophrenia

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ABSTRACT

Medication nonadherence is common in patients with schizophrenia. Nonadherence affects approximately half of all patients and may increase the risk of relapse and hospitalization. Although it is an intensively studied phenomenon, we have little understanding of underlying mechanisms leading to nonadherence. In this article, using quantitative and qualitative study results and psychological decision theory, we present a model of medication adherence decisions in patients with schizophrenia that may be useful for clinicians and those involved in the development of adherence interventions or adherence research. The model focuses on the function and meaning of medication from a patient perspective. Although the model is a simplified description of the decision-making process related to medication use, it does explain the role of some important aspects such as insight, side effects, efficacy, and social influences. We also discuss how this may explain the high and persistent rates of nonadherence. Finally, we discuss some implications for clinical practice.

Prim Care Companion CNS Disord 2017;19(6):17n02182
<https://doi.org/10.4088/PCC.17n02182>

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Schizophrenia is a severe mental disorder for which medication is considered to be the most effective treatment. Half a century ago, Parkes et al¹ and Renton et al² established that 45% of patients with schizophrenia failed to take their medication as instructed. Several studies^{3–6} have shown that the level of nonadherence is still the same today. Systematic reviews^{3–6} have found an average nonadherence prevalence of between 40% and 55%. This means that, despite all the research efforts and the development of adherence interventions and new medications, we have been unable to improve adherence behavior in the last half century. Although extensive research has increased our knowledge, much is still unknown, and breakthroughs have not been achieved. We do know that nonadherence results in an increased risk of relapse and hospitalization and that it is associated with high economic costs.^{7–17} Unfortunately, a clear solution to this problem is not yet found. In this article, we present a model of medication adherence that may be useful in clinical practice.

DETERMINANTS OF NONADHERENCE

A first and indispensable step in finding solutions that really work is understanding why patients stop using their medication. Many studies have been performed to find factors associated with, or predictors of, nonadherence in patients with schizophrenia. Several published reviews^{4,5,18–24} have included a systematic literature search on risk factors. Most of these authors determined that they could not arrive at any conclusions about many of the variables included in their review because the study results were too inconsistent or conflicting. But even between reviewers, there is disagreement concerning which factors do or do not affect adherence, which may be due to different methodologies, study samples, and individual differences. There are, however, several factors for which most reviewers agree that are higher in nonadherent patients such as substance abuse, rates of positive symptoms, disorganization, and symptom severity. Furthermore, most reviewers conclude that adherence is better if patients have insight, positive attitudes toward medication, and belief or experience that medication is effective. A good therapeutic alliance is also consistently associated with medication adherence. Finally, patients who receive no support from their relatives, who live alone, and who do not have supervised medication intake are generally more nonadherent.

Although we know that these factors are associated with nonadherence, few attempts have been made to explain how they relate to patients' decision-making processes. In fact, adherence in patients is often described as a "black box phenomena." As a consequence, our understanding of the mechanisms underlying nonadherence is poor.^{4,25,26} For instance, for most of the factors described, we do not know

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- Clinicians should strive for shared decision-making preceded by an exploration of all pros and cons the patient considers important for his or her well-being.
- Clinicians should pay close attention to medication efficacy, particularly in remitted or poor treatment responders, as evidence indicates that efficacy is one of the most important motivators for patients to use medication.
- Clinicians should explore the role of significant others in medication adherence, as they may act as trusted sources of information, offer practical support with medication intake, or exercise social pressure by encouraging and approving medication adherence.

how or why they influence adherence. The absence of a model that explains the role of all major determinants of nonadherence is considered one of the main problems in adherence research.

A PATIENT-CENTERED MODEL OF MEDICATION ADHERENCE

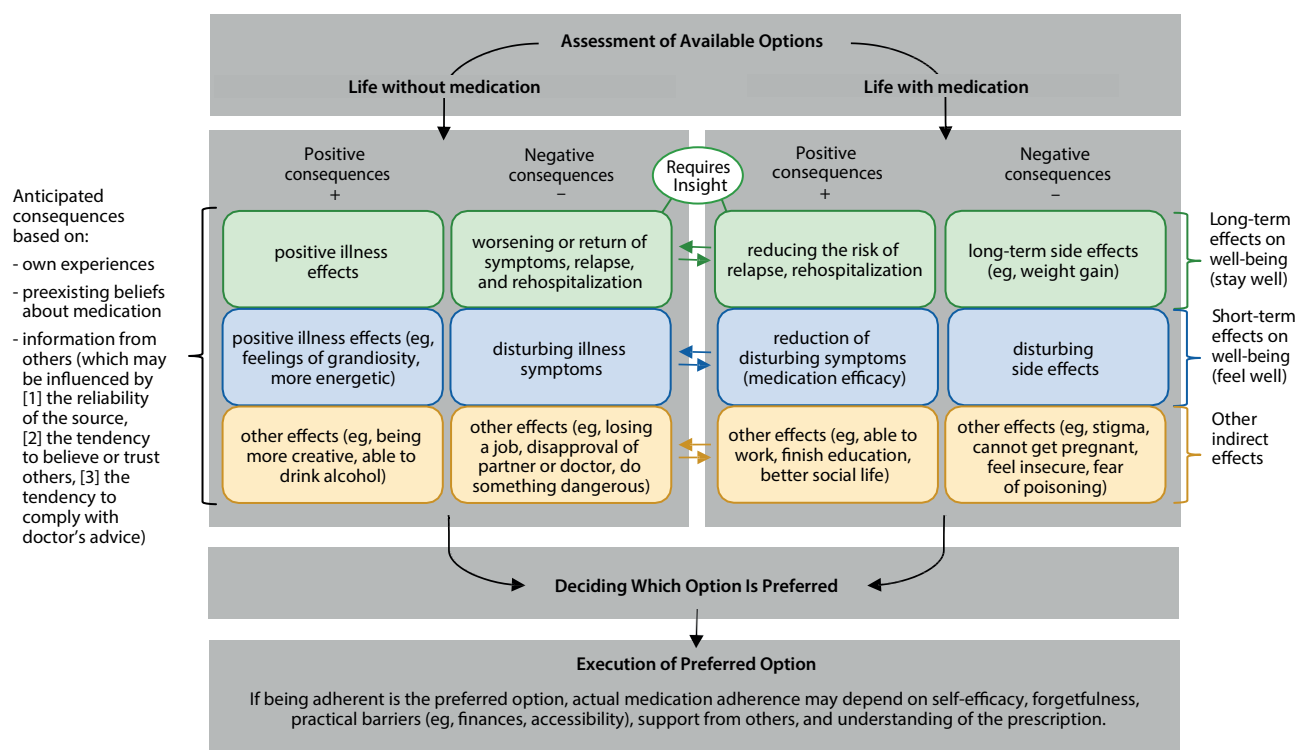
Medication adherence is about the choices made by individual patients. In an attempt to develop a model that gives us insight into these choices, we resort to the different psychological models that have been developed to explain how people make health-related decisions.²⁷ Despite the extensive literature on this topic, there have been few attempts to apply these models to patient decisions about medication use. Exceptions are some older models such

as the Theory of Planned Behavior,²⁸ the Self-Regulatory Model,²⁹ and the Health Belief Model, which is probably the best known.^{30,31} The Health Belief Model has been used by several researchers to explain patient behavior.^{5,32–34} It is a psychological model initially developed to explain the reluctance of people to make use of a health program. It was developed by Becker and colleagues^{30,31} in the 70s and 80s and is based on the value expectancy theory. This theory states that patient behavior depends on the subjective importance of an outcome and the subjective expectation that a particular behavior will achieve that outcome. It is a generic model that we will try to adapt to describe medication decision processes. For this we examined, next to quantitative studies, qualitative studies that focus on medication adherence in schizophrenia. These sources provide more first-person perspective and therefore form a valuable supplement to quantitative studies.

On the basis of the principles of the Health Belief Model, we constructed a patient-centered framework for the key factors related to patient decision-making (Figure 1). This model assumes that for patients, medication is no more or less than a means to achieve the best possible outcome. To do so, patients have to weigh the expected outcomes of the 2 options available to them: taking their prescribed medication or not. Each of these 2 options will have certain benefits and drawbacks, and depending on the importance of each to them and their expected likelihood, they will be more or less inclined to be adherent.

These benefits and drawbacks of medication use can be derived from literature and can be divided into short-term

Figure 1. Patient-Centered Framework for the Key Factors Related to Patient Decision-Making



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or long-term effects of medication on well-being. In other words, patients can take their medication to feel better now or to stay better. Feeling better generally refers to subjective well-being within a timeframe of a few days and how it is affected by medication. An obvious example is the reduction of adverse symptoms such as voices or feelings of anxiety. Staying better refers to the anticipated effects of medication in the long-run. Typically, patients indicate that they use medication to prevent a relapse or rehospitalization, which is also a highly relevant reason for clinicians to prescribe medication. But, besides these direct effects of medication on psychopathology and physical and psychological well-being, other indirect consequences such as social or professional functioning, feelings of autonomy, and the burden of using them may also be perceived as important benefits or drawbacks of medication use.^{35,36}

It has been questioned whether people with a psychotic disorder are capable of making rational decisions as assumed in this model.³⁷ There is, however, no indication that someone stops using rational decision-making strategies when diagnosed with a psychotic disorder. We argue that decision-making in stabilized psychotic patients, not including patients in acute psychosis, is rational but that some patients may incorporate irrational factors into their decision.

SUPPORT FROM QUALITATIVE STUDIES

Interestingly, the basic principles of this model are in line with conclusions drawn in several qualitative studies^{38–44} based on interviews with patients. Carrick et al, for instance, conclude “for patients the decision to take antipsychotic medication is based on how they weigh up the costs and benefits of the medication, not simply in terms of symptom reduction but the combined level of distress caused by those symptoms and/or by side effects.”^{38(p30)} Marland and Cash³⁹ describe 3 types of decision-making: direct-reactive, which focuses on short-term effects on well-being; deferential, in which the patient is more likely to trust and follow the clinician’s advice; and active-discernment, which seeks optimization of the balance between quality of life and the consequences of taking medicine. Also, other qualitative studies confirm the idea that patients do indeed try to predict and weigh benefits and disadvantages of taking medication or not.^{40–44}

ANTICIPATED CONSEQUENCES AND WHERE THEY COME FROM

Patients need information to make an assessment about the benefits and drawbacks of medication use. This can be derived from previous experiences, existing beliefs about medication, and advice or opinions of others. Probably the most important will be first-hand experience—knowing what it is like to use medication and how it affects your well-being. Each patient will have his or her own set of unique circumstances, attitudes toward medication, level

of experience, and tendency to listen and trust the advice of others or to comply with their doctor’s advice. Each patient may therefore link other factors to medication use. It is possible that some of these factors are irrelevant, unrealistic, or based on false assumptions, delusional thoughts, or other misconceptions. Certain factors will be relevant for the majority of patients such as side effects and medication efficacy. But in addition to those factors, we found a large variety of other aspects that were only important for certain individual patients.³⁵ Also, the importance of specific factors varies from patient to patient. For instance, some patients may not take the long-term effects of medication into consideration, while this is a decisive aspect for others.

Some examples of less obvious advantages of medication use, as mentioned by patients, are feeling less aggressive, having less unsettling dreams, feeling less confused, and being able to look after a family member. Some reported disadvantages are agitation, fear of becoming addicted to the medication, the burden of taking the medication every day, feelings of failure, and knowing that the voices will still be there. Examples of advantages of not using medication are feeling more energetic, sleeping better, feeling more spontaneous and sensitive toward the environment, being more creative, being able to drink alcohol, and maybe being able to become pregnant with less risks for one’s unborn child. Disadvantages can be fear of disapproval or disappointment in family members, risk of losing independent housing, and fear of putting oneself in danger or doing something stupid.

Finally, it is often mentioned that social context is an important factor in adherence. Our model shows the different levels at which significant others can influence adherence. First, family and friends may serve as important sources of information about pros and cons of medication use. Second, social pressure, the anticipated negative or positive reaction of significant others, may be taken into account as an indirect consequence of medication use itself. Third, support from others may be needed to help patients in the execution of medication use.

DECISION-MAKING AND ACTUAL MEDICATION USE

Our model is a simplified description of the decision-making process related to medication use. However, whether the result of this process is reflected in patients’ actual behavior depends on other factors. Studies show that patients’ behavior in the end can be affected by practical barriers such as accessibility of the medication and medication costs, self-efficacy, forgetting to take medication, patients’ understanding of the prescription, and the support and attitudes of family members. The outcome of the decision-making process should therefore be seen as a tendency or an attitude toward medication use.

INTERPRETING THE MODEL

The model shows the dynamic and intertwined relationship between some of the negative consequences

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of the illness and medication efficacy, which means that if a patient does not experience any unpleasant symptoms or consequences of his or her illness, medication will have no potential short-term benefit. On the other hand, medication also becomes less appealing if a patient does not expect it to have any beneficial effect in reducing his or her symptoms. Similarly, for the long-term effects, preventing a relapse using medication will only be a consideration in patients who feel susceptible to relapse. This is, in fact, closely related to the concept of insight. Patients who use their medication to prevent a relapse or hospitalization must, at least to some extent, acknowledge that they are not well and that treatment is needed. It is the core concept of insight.⁴⁵⁻⁴⁷ In contrast, short-term effects on well-being do not require insight in order to be acknowledged. Patients may take medication simply because it makes them feel better, even if they reject the idea of having a psychotic disorder. This reasoning may help explain why some studies show that insight is an important predictor of medication adherence but that patients without insight can still be adherent.^{5,48}

Although the importance of factors will vary between patients, there are some clear trends. In adherence literature and in clinical practice, the importance of side effects is often emphasized. This emphasis is correct since side effects are probably the most important factor leading to nonadherence. However, when given a choice, overwhelming evidence from a wide variety of studies^{14,35,42,49-59} demonstrates that, according to patients, the subjective efficacy of medication is a more important factor in medication adherence. This subjective efficacy is also reflected in the association between adherence and positive attitudes toward medication and the belief that medication is effective, as found in several reviews.^{5,21} The above-mentioned literature clearly shows the importance of medication efficacy, which indicates that the possibility to get rid of or reduce symptoms is one of the strongest motivators for patients to use medication. This is relevant in discussing adherence issues with patients but may also help explain why the 2 mechanisms discussed in the next section make it so difficult to improve adherence in a relatively large group of patients.

EXPLAINING PERSISTENT RATES OF NONADHERENCE

First, in 55% of patients, psychotic episodes are followed by periods of remission in which psychotic symptoms are absent. Some of these patients undergo partial remission and have negative symptoms, anxiety, or depression.⁶⁰ Since antipsychotic medication primarily affects positive symptoms, nonadherence during periods of remission may have few, if any, direct consequences on well-being for patients. This concept was demonstrated by a study⁶¹ of 65 remitted patients with schizophrenia. In this study,⁶¹ guided discontinuation of antipsychotic medication after a first psychotic episode was successful in 22% of patients in an average follow-up period of 13.2 months. In 32% of patients, medication was discontinued for a mean of 5.0 months,

after which medication was restarted because of relapse or mild recurrent symptoms. In this study,⁶¹ discontinuation was not feasible in 46% of patients due to exacerbation of symptoms during tapering of the dosage. Results show that 54% of patients could have been fully nonadherent with no noticeable consequences for several months up to more than 1 year.

Second, once medication is taken by the patient, both pharmacokinetic and pharmacodynamic factors can interfere with the desired therapeutic effects, resulting in nonoptimal or suboptimal treatment response. Studies⁶²⁻⁶⁴ have found this phenomenon in approximately one-third of patients with schizophrenia. In a survey⁶⁵ of 205 inpatients and outpatients with schizophrenia in Amsterdam, 27% of patients reported that the reduction of symptoms through medication was unsatisfactory, and 51% reported persistent symptoms.

Clearly, remitted and nonresponding patients, together a substantial proportion of schizophrenia patients, do not fully or partially enjoy one of the most important benefits of medication: the reduction of adverse symptoms. For these patients, the benefits of medication may not outweigh possible disadvantages such as side effects and burden of taking the medications, and, consequently, it may make a lot of sense not to take medication.

CLINICAL PRACTICE

The proposed model is not designed as an intervention tool but may be useful in clinical practice when discussing medication adherence issues with patients. It can help clinicians to target their questions. To ensure that all relevant factors are discussed, a good starting point may be to explore all the boxes in the model with the patient. Discussion of positive and negative aspects of using and not using medication with a patient is in fact a technique often used in motivational adherence interventions.^{66,67} Exploration of patients' expectations about the consequences of taking or not taking their medication may help to understand patient behavior, to generate an insight into their perception of the function and meaning of medication, and to identify obstacles to medication use or patient misconceptions. To do so, it may also be relevant to know whether these expectations are based on their own experiences or hearsay. As stated previously, knowing why a patient is reluctant or unable to use medication as prescribed is a first and important step in finding a solution. Each underlying problem may require a different approach such as motivational interviewing techniques, changing medication regimen, involving family members, improving illness insight, or providing practical support in the execution of medication intake.

In addition, showing an interest in patient thinking and concerns shifts the focus away from the medication adherence itself toward aspects that are relevant for the patient. Consequently, it is likely to further the therapeutic relationship, which is associated with successful outcome

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and improved adherence.^{68–72} Finally, the next logical step is to involve patients actively in treatment decisions. There is substantial evidence that shared decision-making is effective in improving adherence in chronic illnesses, including psychiatric conditions,^{73–75} and may include discussing changing medication or dosing or even discontinuing medication if desired.⁷⁶ The latter is an option that more and more clinicians and researchers are now looking into. From a patient's perspective, shared decision-making may make a lot of sense and is likely to increase willingness to use medication when needed. In those cases, however, the term *medication adherence* is somewhat inappropriate. If a patient and his or her clinician agree to discontinue medication, adherence refers not to the use of medication but to the agreed treatment, which may involve active monitoring, appointment schedules, and a crisis plan.

Although the importance of discussing the subjective perception of symptoms and medication effects seems to be common sense, several studies^{40,77} suggest that it is often not common practice among clinicians. A survey⁷⁸ among patients with schizophrenia and schizoaffective disorder showed that a discussion about potential side effects or about how the medication works took place in only 49% and 30% of patients, respectively, and no more than 36% of patients were given a choice about the type of medication. Another indication of the limited quality of the dialogue about medication comes from studies^{79,80} demonstrating that

treating clinicians are, on average, not good at estimating the degree of adherence.

CONCLUSION

An important first step in finding solutions for nonadherence is understanding patient motives for taking or not taking prescribed medication or not. On the basis of our results, as well as those from other qualitative and quantitative studies, we argue that patients' primary motives for taking medication are a subjective improvement in well-being and the reduced risk of relapse. These factors are offset against the negative consequences of using medication, such as side effects and loss of autonomy. For patients, adherence is a means to an end. If medication reduces well-being, which is likely in some cases, patients are more prone to becoming nonadherent. Research is warranted to further our understanding of the underlying mechanisms of adherence and to explore patient perspectives. To achieve this goal, qualitative studies seem to be useful to supplement the existing literature and quantitative studies. Future research should also examine the quality of the dialogue patients have with their clinician about medication-related thoughts and concerns. If time is taken to explore these areas in clinical practice, clinicians will be able to tailor adherence interventions. This approach is also likely to improve adherence by enhancing the therapeutic alliance.

Submitted: June 20, 2017; accepted October 6, 2017.

Published online: December 7, 2017.

Potential conflicts of interest: None.

Funding/support: None.

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