

## Medication Adherence in Schizophrenia: Exploring Patients', Carers' and Professionals' Views

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**One of the major clinical problems in the treatment of people with schizophrenia is suboptimal medication adherence. Most research focusing on determinants of nonadherence use quantitative research methods. These studies have some important limitations in exploring the decision-making process of patients concerning medication. In this study we explore factors influencing medication adherence behavior in people with schizophrenia using concept mapping. Concept mapping is a structured qualitative method and was performed in 4 European countries. Participants were 27 patients with schizophrenia, 29 carers, and 28 professionals of patients with schizophrenia. Five clinically relevant themes were identified that affect adherence: medication efficacy, external factors (such as patient support and therapeutic alliance), insight, side effects, and attitudes toward medication. Importance ratings of these factors differed significantly between professionals and carers and patients. Professionals, carers, and patients do not have a shared understanding of which factors are important in patients' medication adherence behavior. Adherence may be positively influenced if professionals focus on the positive aspects of medication, on enhancing insight, and on fostering a positive therapeutic relationship with patients and carers.**

*Key words:* medication adherence/schizophrenia/  
concept mapping

### Introduction

Treatment nonadherence limits the clinical effectiveness of prescribed medication.<sup>1</sup> Studies often report that about 50% of patients are treatment nonadherent across a range of disorders.<sup>2</sup> Different authors, often using a quantitative approach, generally present a range of factors that influence treatment adherence with medication in patients with schizophrenia.<sup>3–7</sup> Consistently reported factors include insight, beliefs about treatment, medication side effects, and treatment efficacy.<sup>3</sup> Although research has improved our knowledge, adherence rates do not seem to have changed in the last 4 decades.<sup>8,9</sup>

More recently, interventions focused on nonadherence were developed. Several researchers have proposed that these adherence interventions should focus more on patients' decision-making process.<sup>6,10</sup> For this, quantitative studies have some, but limited, value because they fail to adequately explain the complexity of medication-taking behavior and are only able to explore a limited number of variables.

Other more qualitative studies have tried to describe adherence behavior by focusing on the subjective responses or experiences of patients with antipsychotic medications and their decision-making process in relation to starting, continuing, or stopping medication. Conclusions regarding which factors influence adherence behavior are often based on either patients'<sup>11–14</sup> or professionals' views.<sup>15</sup> These views might differ as we know from research in other fields. Fischer et al,<sup>16</sup> for instance, showed that patients', carers', and professionals' views concerning outcome and service priorities vary widely. Similar conclusions were drawn by Pope and Scott,<sup>17</sup> studying main reasons to stop medication treatment in patients receiving lithium for an affective disorder. To increase our understanding of medication adherence, we should make use of the valuable expertise and experience of different stakeholder groups. Relying solely on one of these groups might give limited and unsatisfactory results.

The aim of this article is to learn more about (non)adherence in patients with schizophrenia. For this, we will use concept mapping, an established qualitative methodology, to explore factors that influence adherence behavior in patients with schizophrenia. We will include the opinions of patients, carers, and professionals from 4 countries.

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## Materials and Methods

### Setting

This study was conducted in 4 European Union countries: England, Germany, Italy and the Netherlands. It was part of the quality of life following adherence therapy for people disabled by schizophrenia and their carers (QUATRO) study, an international multisite randomized controlled trial assessing the effectiveness of adherence therapy in people with schizophrenia. All study sites gained full approval for the study from the appropriate local research ethics committee.

### Participants

Participants were purposively selected out of the 3 stakeholder groups. Patients were meeting International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) criterion for schizophrenia. Carers and professionals were, respectively, caring for and working with patients with schizophrenia. All participants needed to be familiar with positive and negative consequences of antipsychotic medication. Therefore, patients needed to have had antipsychotic medication prescribed to them for at least 1 year. Carers and professionals needed to care for or work with patients with schizophrenia for a period of at least 2 years. Participants should have experience with non-adherence. Although the majority of patients and, consequently, their carers go through a nonadherent period during the course of their illness,<sup>6,18</sup> patients were only included if they had been clinically instable in the previous year. This was defined by one or more of the following: at least one hospital admission on clinical (mental health) grounds, a change in antipsychotic medication, increased frequency of planned or actual contact, and indications of clinical instability from relatives, carers, or clinical team. These criteria were considered indicative of nonadherence. Carers were included if they were caring for patients fulfilling inclusion criteria. All participants were further expected to be able to adequately verbalize ideas and thoughts concerning medication adherence and perform the required tasks. A high-quality systematic review indicated that other sociodemographic characteristics have no influence on medication adherence<sup>3</sup> and were therefore not assessed in this study. In order to increase variability of generated statements and generalizability of our results, stakeholder groups were unrelated. All participants gave written informed consent.

### Procedure

To study variables or factors that (positively or negatively) influence patients, medication adherence behavior concept mapping was used. This method uses group discussions with patients, carers, and professionals to

explore factors related to medication adherence. In contrast to other qualitative methods it also comprises a clustering and a prioritizing task. The clustering task allows for the participants to determine which factors or clusters emerge from the data and to what extent these clusters are related to each other. Therefore, compared with other qualitative research methods, the interpretation of the qualitative data might be less susceptible to the hypothesis that researchers may have. The prioritizing task enables, using a quantitative methodology, a comparison of the relative importance stakeholder groups address to the different factors or clusters.<sup>19,20</sup>

The procedure was administered by a trained facilitator and cofacilitator in each country. Concept mapping consists of 4 stages. For each stage, a written protocol was provided to make sure all sites followed the same procedure. A copy of the manual can be requested from the first author.

During the first stage, brainstorming sessions were held separately for patients, carers, and professionals in each of the 4 sites. According to Concept Mapping protocol,<sup>21</sup> each of these 12 sessions were attended by 6–9 participants and took approximately 1.5 hours. Due to having 12 sessions, our study sample exceeded that of typical concept-mapping studies in which it is between 10 and 20.<sup>19</sup> Patients were invited to generate statements focusing on “all factors that influence whether you take or not take antipsychotic medication.” Carers and professionals were asked to generate statements on “all factors influencing the start and continued use of antipsychotic medication.” If patients were inhibited to verbalize their thoughts, they were invited to submit statements in writing or on a one-to-one basis after the session finished.

In the second stage, the number of generated statements had to be reduced to below 100 in order to control the complexity of the following steps. After translation into English, 5 researchers (not involved in the brainstorming sessions) independently reviewed all generated statements. Statements that were not understandable, not singular, too specific, or too abstract were removed. Next, repetitive or overlapping statements were combined into single statements. Finally, in each country, the remaining statements were reviewed and rated by researchers according to how well each related to the topic of medication adherence on a 3-point scale. Those rated least relevant were excluded, leaving a final list of statements. These were back-translated into German, Italian, and Dutch. Translations were conducted according to WHO guidelines.<sup>22</sup>

Finally, in the third and fourth stage of the concept-mapping procedure, statements had to be clustered and prioritized. Groups were reconvened, and participants were asked to individually perform the remaining tasks. First, participants had to organize the statements they thought belonged to the same category into clusters

(stage three). Clustering could be done in any way the participant thought was logical. Each cluster had to contain between 5 and 40 statements. In addition, individual participants were asked to prioritize the statements (stage four) by sorting them into 5 equal piles, ranging from least to most important. Patients were asked how important each aspect was for their decision to take or not take antipsychotic medication, and carers and professionals were asked to rate how important they thought each aspect was for patients.

#### Data Analysis

The “Ariadne” software package was used to perform 2 types of analysis.<sup>21</sup> The first, a principal component analysis, positions the statements on a concept map. Here the distance between statements represents how often they have been sorted together. Secondly, a cluster analysis grouped statements in clusters. This analysis produced between 2 and 18 clusters. Three researchers independently reviewed each of these 17 computer-generated cluster solutions starting with the simplest (ie, 2 clusters) and ending with the most complex (ie, 18 clusters). The cluster solution that was most understandable and meaningful was selected.

Finally, the relative importance of each cluster was calculated using the prioritizing data. For each participant, the percentage of statements, in each cluster, rated 4 or 5 (important) was calculated. Differences in means were tested using analysis of variance.

## Results

Brainstorming sessions were attended by 91 participants (41% male) and the prioritizing and clustering sessions by 89 participants (44% male), approximately equally divided over the 4 sites (table 1). Results of 4 patients and 1 carer across 3 sites were removed from the data set. These participants indicated they found the clustering and/or prioritizing task too complicated. They also did not profit from support, and their results clearly demonstrated their lack of understanding (eg, statements clustered according to card number instead of contents).

On average, patients ( $n = 27$ ; 59% male) had been prescribed antipsychotic medication for a period of 8.6 years ( $SD = 8.2$ ). Carers ( $n = 29$ ; 28% male) had been caring for someone with schizophrenia for an average of 12.6 ( $SD = 7.4$ ) years, and professionals ( $n = 28$ ; 46% male) had been working with patients with schizophrenia for an average of 11.4 ( $SD = 11.1$ ) years.

#### Brainstorming

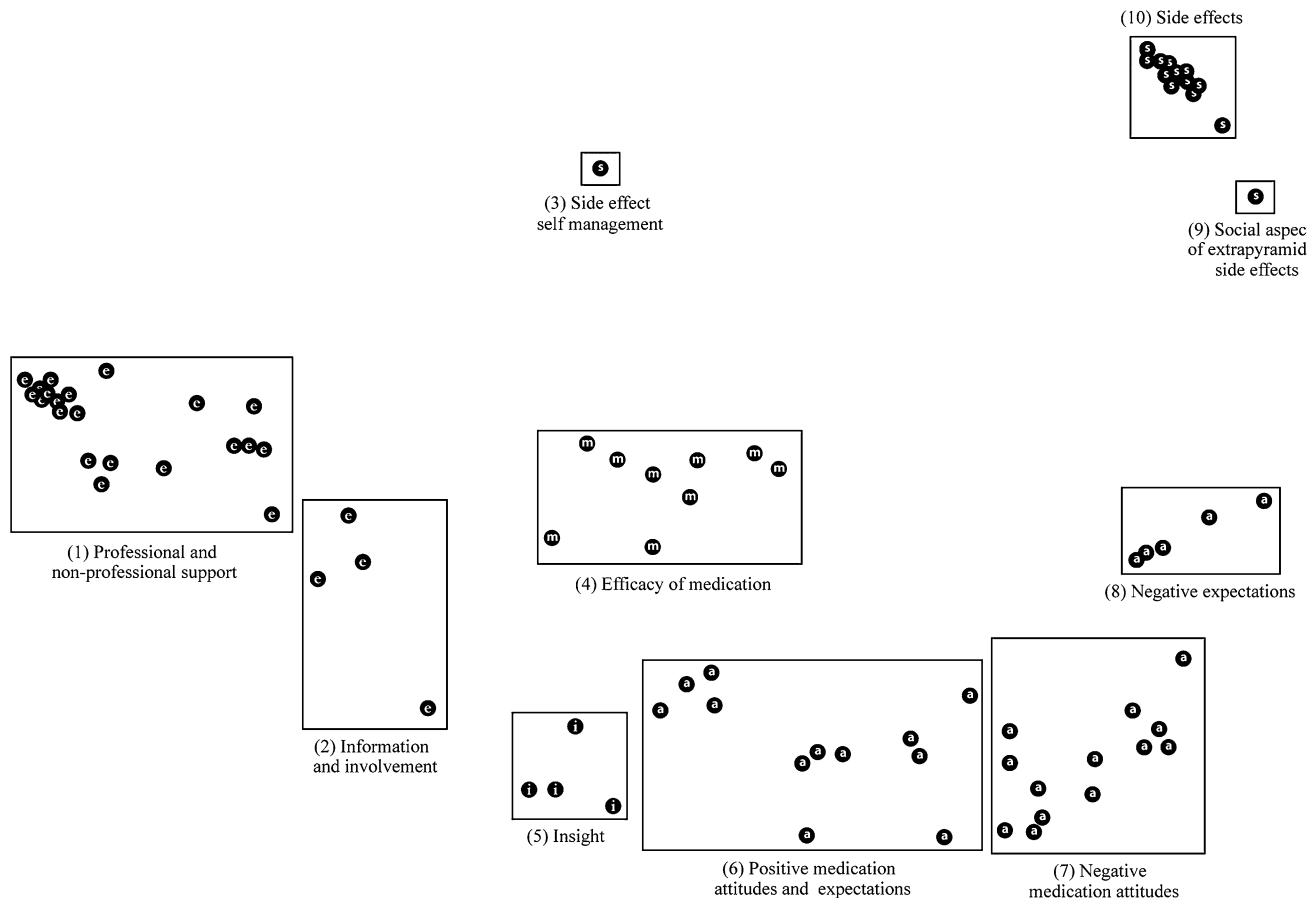
The 12 brainstorming sessions produced a total of 769 statements relating to factors influencing medication adherence for patients with schizophrenia. Generated statements confirmed that participants were familiar with both positive and negative aspects of antipsychotic medication. Out of all the statements generated by patients, carers, and professionals, respectively, 48%, 42%, and 51% were negative aspects of medication use. Following translation, researchers reached consensus on the elimination of 141 statements not meeting the criteria and combined 424 statements with other statements because they were repetitive or overlapping. The amount of overlap indicated issues reaching a point of saturation. The remaining 204 statements were rated, resulting in a final set of 82 statements, of which approximately equal numbers of statements were found to be produced by the 3 stakeholder groups (56% of statements were mentioned by patients, 56% by carers, and 66% by professionals) and across the 4 sites.

#### Clustering

All statements are presented as dots on the concept map in figure 1. Their spatial position is based on the clustering results. Statements that the participants sorted together more frequently are positioned closer to each other on the concept map. Consequently, the distances between the statements in figure 1 indicate to what extent, according to the participants, statements and, consequently, clusters are related to each other. On the basis of these interstatement distances, clusters are defined. A 10-cluster solution was considered to be most understandable and meaningful. A cluster solution with fewer clusters resulted in the loss of clinically relevant clusters.

**Table 1.** Participants in Brainstorming Session (BS) and Clustering and Prioritizing Tasks (CP)

	Patients		Carers		Professionals		Total	
	BS	CP	BS	CP	BS	CP	BS	CP
Amsterdam	6	6	6	7	8	8	20	21
Leipzig	9	6	7	7	6	4	22	17
London	7	7	8	7	9	8	24	22
Verona	8	8	8	8	9	8	25	24
Total	30	27	29	29	32	28	91	84



**Fig. 1.** Concept map of factors influencing medication adherence for patients with schizophrenia. The map displays the 82 statements as dots, the 10 clusters, and 5 clinical themes; medication efficacy (m), external factors (e), insight (i), side effects (s), and medication attitudes (a). Distance between statements indicates how often they have been sorted together.

Cluster solutions with more clusters were difficult to interpret and resulted in clusters that were considered less meaningful. Clusters that were located close to each other referred to distinct but clinically related topics. Clusters on the map were numbered from left to right and labeled. Examples of statements are shown in table 2.

### Prioritizing

Table 3 shows the average percentages of statements in each cluster which were rated as important by patients, carers, and professionals. There was general agreement between patient and carer ratings of the relative importance of each cluster. However, there were a number of significant differences between patient and/or carer and professional ratings. The latter rated the efficacy of medication (cluster 4) as significantly less important and negative medication attitudes and beliefs (cluster 7) as more important cluster than carers and patients. The professional and nonprofessional support cluster (cluster 1) was rated as less important and the side effect cluster (cluster 10) as more important by professionals compared with carers.

### Discussion

In this study, we used concept mapping to explore “all factors influencing the start and continued use of antipsychotic medication” comprehensively by including 3 different and independent groups of stakeholders, all familiar with schizophrenia for many years, from 4 different countries. In this discussion, we will interpret our results and describe its clinical and research implications.

Content and spatial location of the clusters are used to interpret the concept map and identify clinically relevant themes (figure 1). Statements, except those in clusters 1, 2, and 5, referred to perceived advantages or disadvantages of medication use and were divided into 3 themes; right in the middle we identified medication efficacy (cluster 4), surrounded clockwise by issues related to side effects (clusters 3, 9, and 10) and attitudes (clusters 6, 7, and 8). Although closely located, due to the content of the statements, insight (cluster 5) is considered a separate theme in this concept map. The remaining clusters 1 and 2, both distant from the other clusters, referred to external factors.

**Table 2.** Cluster Number, Cluster Label, and Examples of Statements

Cluster Number and Label	Examples of Statements
1: Professional and nonprofessional support	<p>“being accurately informed about the potential side effects of the medication”</p> <p>“the doctor asking you how you feel, being understanding and listening to your concerns”</p> <p>“family, friends remind you to take your medication”</p> <p>“accessibility of the medication (getting the prescription and medication on time)”</p>
2: Information and involvement	<p>“being given the choice whether or not to take medication”</p> <p>“listening to other patients experiences of taking medication”</p> <p>“not being told what your diagnosis is”</p> <p>“having an understanding of the illness”</p>
3: Side effect self-management	<p>“knowing how to manage the side effects”</p>
4: Efficacy of medication	<p>“being able to function better due to the medication”</p> <p>“the medication is effective in reducing the hallucinations”</p> <p>“the medication keeps you from feeling ill/ relapsing”</p>
5: Insight	<p>“having insight into the illness”</p> <p>“accepting that medication is needed”</p> <p>“your cultural beliefs fit in with medical advice”</p>
6: Positive medication attitudes and expectations	<p>“having faith that the medication is effective”</p> <p>“taking medication to avoid going back into hospital”</p> <p>“good previous experiences with medication”</p>
7: Negative medication attitudes	<p>“feeling suspicious about the medication”</p> <p>“believe that the medication will harm you”</p> <p>“the voices telling you not to take the medication”</p> <p>“believe that taking medication is unnatural”</p>
8: Negative expectations	<p>“feeling better when you stop taking it”</p> <p>“a traumatic experience the first time you were given medication”</p> <p>“preferring the symptoms to the side effects”</p>
9: Social aspects of extrapyramidal side effects	<p>“being embarrassed about movement disorders because people can see it”</p>
10: Side effects	<p>“obesity/weight gain due to the medication”</p> <p>“sexual problems due to the medication”</p> <p>“feeling tired due to the medication”</p>

### *Efficacy*

Cluster 4 represents the subjective efficacy of medication due to a relief of symptoms. Patients and carers both rated this cluster as the most important for medication adherence. This is in line with authors showing that the beneficial effects of medication on well-being have a major influence on adherence behavior.<sup>14,23–25</sup> Accordingly, studies showed that patients who have the experience of their medications having no benefit, not being helpful, or being ineffective and unnecessary more often do not comply.<sup>18,26–29</sup>

Professionals in our study surprisingly rated efficacy significantly less important than patients and carers. Professionals should (re)value efficacy as more important and are advised to closely monitor and discuss medication efficacy, from the patients perspective, as well as the perceived degree (or absence) of adverse symptoms, in order to understand and manage medication adherence.

### *External Factors*

Clusters 1 (professional and nonprofessional support) and 2 (information and involvement) contain statements that refer to factors which contribute to establishing favorable conditions for adherence behavior by different means, such as increasing patients understanding, alliance, or trust with clinician; social support; and reduction of practical medication barriers. These factors can be labeled as external because they refer to influences from outside by important others, not directly under the control of the patient. Both clusters adjoin but are distant from the other clusters in the concept map, suggesting that they are not strongly related to the other clusters.

Nonprofessional (or professional) support, information, and involvement have been studied as important predictors of treatment adherence in people with schizophrenia.<sup>30–34</sup> Some psychological approaches enhancing treatment adherence have placed them at the heart of the

**Table 3.** Mean Percentage of Items Per Cluster Rated 4 or 5 (important), Stratified by Patients (Pa), Carers (Ca) and Professionals (Pr)

Cluster Number and Label	Number of Statements	Pa ( <i>n</i> = 27)		Ca ( <i>n</i> = 29)		Pr ( <i>n</i> = 28)		<i>p</i> < 0.05 <sup>c</sup>
		Mean <sup>a</sup> (%) (SD)	<i>r</i> <sup>b</sup>	Mean <sup>a</sup> (%) (SD)	<i>r</i> <sup>b</sup>	Mean <sup>a</sup> (%) (SD)	<i>r</i> <sup>b</sup>	
4: Efficacy of medication	9	54 (20)	1	64 (23)	1	40 (21)	5	Pa-Pr; Ca-Pr
3: Side effect self-management	1	48 (51)	2	34 (48)	6	39 (50)	6/7	
5: Insight	4	44 (19)	3	54 (21)	2	52 (23)	1	
1: Professional and nonprofessional support	21	42 (12)	4/5	52 (16)	3	37 (15)	8/9	Ca-Pr
6: Positive medication attitudes and expectations	12	42 (14)	4/5	36 (14)	4/5	36 (12)	10	
10: Side effects	12	40 (21)	6	28 (19)	8/9	46 (24)	2	Ca-Pr
2: Information and involvement	4	39 (22)	7	36 (21)	4/5	37 (24)	8/9	
8: Negative expectations	5	36 (22)	8	32 (18)	7	43 (22)	3	
7: Negative medication attitudes	13	30 (13)	9	25 (16)	10	42 (14)	4	Pa-Pr; Ca-Pr
9: Social aspects of extrapyramidal side effects	1	22 (42)	10	28 (45)	8/9	39 (50)	6/7	

<sup>a</sup>For each participant, the percentage of statements rated 4 or 5 (important) in each cluster was calculated. The mean percentages over raters are reported in the table (eg, patients rated on average 54% of the nine statements in cluster 4 as important).

<sup>b</sup>Rank order of cluster based on mean percentage.

<sup>c</sup>Analysis of variance, multiple comparisons (Tukey's honestly significant difference test).

intervention,<sup>10,35</sup> which is in accordance with our finding that patients and, in particular, carers rated support, information, and involvement as rather important. So far, compliance interventions focused on education and information have not been found to be effective in improving adherence.<sup>10</sup> This might explain why professionals rate these issues as less important.<sup>36</sup>

### Insight

The map shows that insight (cluster 5) is closely related to positive expectations and attitudes toward the use of antipsychotic medication (cluster 6). All groups rated the insight cluster as important, which is in line with studies describing insight as a strong predictor of medication adherence.<sup>3,37-39</sup> This effect of insight has been addressed to an improvement in understanding illness and medication consequences. The spatial locations of clusters 4 and 5 show that a clear relation with medication efficacy (cluster 4) is, however, lacking. Insight seems less important for appreciating subjective symptom relief due to medication than for indirect treatment benefit such as hospitalization or coercion. A patient who uses his or her medication because it improves well-being does not necessarily need to have insight into the disorder. This might

also explain why Nageotte et al<sup>40</sup> found that 38% of patients were compliant despite the fact that they did not believe themselves to be ill.

### Side Effects

Statements related to side effects that referred to objective perceived side effects of medication (cluster 10), the social aspects of side effects (in particular, movement disorders) (cluster 9), and self-management of side effects (cluster 3). The latter cluster referred to a positive characteristic, which patients rated as very important.

Medication side effects have often been associated with nonadherence,<sup>24,41,42</sup> although a consistent correlation between the presence or severity of these and the degree of adherence could not be found in a recent systematic review.<sup>3</sup> Side effects might not be the most important factor in determining adherence behavior<sup>25,39-43</sup> and may have less impact than the efficacy of medication<sup>44-46</sup> or expressed beliefs concerning susceptibility to relapse.<sup>26</sup>

Our results confirm this and show that patients and carers prioritized side effects relatively low compared with positive medication aspects. In comparison, professionals prioritized side effects as the second most important cluster and, consequently, seem to overestimate the

relative importance of side effects on adherence behavior. Although discussing side effects is essential during treatment because it is the most important disadvantage of medication use for patients, professionals might, however, understand the relative importance better in relation to other factors such as perceived advantages of medication, and coping strategies are taken into account.

### *Medication Attitudes*

Finally, the clusters 6, 7, and 8 represent not only beliefs and attitudes concerning medication but also previous experiences with these agents. Statements of cluster 6 represent positive aspects or benefits of medication (eg, reducing adverse consequences of being ill such as hospitalization or coercion). Clusters 7 and 8 refer to negative attitudes and beliefs concerning medication and feeling better without medication. Different authors have stressed that both attitudes to medication and side effects have to be openly discussed with patients.<sup>25,47</sup>

### *Prioritizing*

Patients were instructed to rate the importance of statements based on their own experiences. Carers and professionals rated statements based on their observations of, and experiences with, patients. Two points are of interest. First, professionals, in general, rated negative aspects (side effects and negative medication attitudes) as more important than patients and carers, while patients and carers, more than professionals, stressed the positive aspects (efficacy and support). Secondly, the fact that carers and patients in our study prioritized clusters in a similar way indicates that carers can be well aware of patients' considerations concerning medication. Our results underline that professionals need to carefully assess patients' beliefs and experiences of treatment with antipsychotic medication in order to understand patients' perspectives. They also, if possible, should involve carers in treatment planning and evaluation. Not only will it improve patients' support, which was found to be an important issue, but also carers might be able to provide professionals with valuable information.

### *Models for Understanding Adherence*

Our results correspond with the Health Belief Model, often used to explain adherence behavior.<sup>48</sup> According to this model, individuals' readiness to take action depends on their "perceived seriousness and susceptibility of illness" (such as belief in the accuracy of the diagnosis and subjective vulnerability to relapse) and "perceived benefits and barriers of medication use." This is reflected in the themes insight, efficacy of medication, side effects, and medication attitudes. These themes demonstrate patients' considerations concerning advantages and disadvantages of medication use. Contrary to the Health

Belief Model, we did not find perceived illness severity and medication benefit to be separate themes (eg, "the medication is effective in reducing the hallucinations").

We argue that patients are most motivated to use medication if they experience direct beneficial effects such as a reduction of adverse symptoms and/or because they realize it has indirect, long-term benefits such as preventing relapse. Although illness insight is not clearly positioned in the Health Belief Model, our results seem to indicate that insight is particularly important for patients to understand and appreciate the indirect benefit of medication. Therefore, patients who experience no direct subjective benefit from medication are most likely to benefit from psychoeducation or brief cognitive behavioral therapy to enhance insight.<sup>49</sup>

The external factors show us that there are a number of factors which are not under patient control, but which might affect adherent behavior. These factors include the alliance between carers and their key worker, the information given to patients, actively involving patients in treatment, and practical medication barriers. These factors are similar to "cues to action" in the Health Belief Model. Clinicians should therefore make every effort to inform patients concerning their illness and medication, increase patients understanding, their alliance with their patient, the provision of social support, and reduction of practical medication barriers.

Results of this study might be useful in screening patients with schizophrenia. Discussing the topics that were found in this study should help professionals to detect patients likely to be nonadherent.

### *Limitations*

This study has some limitations. First, it should be noted that results are limited to issues which were involved in the decision-making process of patients. Therefore, factors which have been found to correlate with adherent behavior such as sociodemographic characteristics and previous nonadherence are not reported in this study. Patient reports are limited to issues they are aware of and they are prepared to mention.

We included a heterogeneous sample of 91 participants. Although this is in accordance with the concept map protocol, this number is relatively low for analysis of between-group differences. However, differences were significant even with this low numbers per group.

Patients were selected if they had been clinically unstable for some period of time within the previous year. This inclusion criterion might have influenced our results because these patients may have stressed the importance of factors that negatively influence medication adherence.

### **Conclusion**

In conclusion, this study has learned that concept mapping is a useful tool in exploring relevant issues for

patients' decision to use or not use prescribed antipsychotic medication. The findings suggest that patients, carers, and professionals were able to identify and weigh up the factors that influence treatment adherence. Our findings provide a comprehensive overview of all relevant issues and how they relate to one another. Clusters could be organized into 5 clinically relevant themes: efficacy of medication, external factors, insight, side effects, and medication attitudes.

The discrepancies between patients' and professionals' views on the importance of clusters should be further explored in future research. Professionals need to be aware of patients' considerations concerning their antipsychotic medication, in particular positive aspects of medication use, in order to provide effective support and guidance. Consequently, strengthening mutual understanding and alliance could improve adherence or make it easier to come to agreements on individually tailored medication regimens. Therefore, closing the gap between patients' and professionals' views on the importance of medication-related aspects seems vital.

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