Relapse prevention in patients with schizophrenia:

A nursing intervention study

Berno van Meijel

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Relapse prevention in patients with schizophrenia:

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Terugvalpreventie bij patiënten met schizofrenie:
Een verpleegkundige interventiestudie

(met een samenvatting in het Nederlands)

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Voor Vonneke

Sam, Tom & Bob

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Chapter 1

Introduction

Introduction

'When my symptoms surface, they come in a series of successive phases all accompanied by physical and emotional side effects. The first phase is the most important: if I don't take steps to control the situation, then each subsequent phase becomes more difficult. In the first phase, I feel somewhat alienated from myself. From my viewpoint, everything seems to be more clear-cut and rigid and my voice seems to reverberate a bit. I then start to feel uncomfortable around other people. In the second phase, everything seems blurred. The blurriness intensifies, as do my confusion and anxiety. I'm particularly afraid of letting others see that there's something wrong. I try to think of some good excuses and to take control of the small things in life. I start to give the wrong interpretation to the way people behave towards me, which increases my fear of losing control. In the third phase, I think that I'm starting to understand why terrible things are happening to me: others are to blame. This conviction is accompanied by the ability to see more clearly, an increased sensitivity to sounds and an increased susceptibility to the way others look at me. I start wondering whether things are true. In the fourth phase, I become chaotic and see, hear and believe in all kinds of things. I no longer doubt my beliefs. Instead I act on them.'

This is the story of a patient who was diagnosed with schizophrenia at the age of seventeen (Lovejoy 1984). Over the years, she underwent therapy regularly both as an in-patient and an outpatient. She experienced several psychotic episodes, marked by delusions and hallucinations. Her contact with reality was seriously disturbed as a result of the psychotic perceptions. She describes in clear terms how her psychoses develop, what she experiences during this process and how she tries to deal with the increasingly serious symptoms. Her account shows quite clearly that her psychotic episodes develop gradually. The relapse process begins with vague, non-specific symptoms and ends in remarkable beliefs and perceptions, which no longer have a basis in reality.

The gradual process leading up to a psychotic episode offers possibilities for preventive intervention. If action is taken at an early stage of the relapse process, a psychotic crisis may be averted. That, in a nutshell, is the essence of this thesis. Its subject is the development and testing of a nursing intervention protocol, aimed at recognizing the early warning signs of a psychotic relapse. Proper intervention following such early recognition might prevent the onset of a serious psychotic crisis.

The study was started in 1996, out of the realisation that if more attention were paid to preventing psychotic relapse, it might lead to a greater standard of health for the patient. Not only would preventive action spare a great deal of personal suffering, it could also contribute to the self-management of the illness by the patient and his family.

The various studies on which this thesis is based were carried out by the Department of Nursing Science (part of the Julius Center for Health Sciences and Primary Care) in collaboration with the Division of Neuro-Science. Both divisions are part of the University Medical Center Utrecht (The Netherlands).

This chapter will start with a short introduction on the psychiatric disorder, schizophrenia. We shall focus on the clinical features and the course of the disorder, in view of their importance for this study. We shall then briefly address the process of psychotic relapse and discuss the concepts of 'early recognition' and 'early intervention'. Finally, we shall describe the structure of this thesis.

Schizophrenia: Clinical Features

Schizophrenia is considered one of the so-called 'major psychiatric disorders' - a description that immediately conveys its serious nature. It is a disorder that occurs frequently. The lifetime prevalence of schizophrenia is estimated to be approximately 0.8% (Bromet & Fennig 1999; Buchanan & Carpenter 2000). Schizophrenia affects various psychological functions, for example perception (hallucinations), ideation and reality-testing (delusions), formal thought processes (loose associations), feeling (flatness, inappropriate affect), behaviour (catatonia, disorganization), attention, concentration, motivation (avolition, impaired intention and planning), and judgement (APA 1997). No single symptom is pathognomonic of schizophrenia. There is an extreme heterogeneity in symptomatology between patients, as well as a large variability of symptoms in individual patients in the course of time. The symptoms cause considerable constraints and impediments in various fields of everyday life, including study and work, self-care, living skills, social contacts and interpersonal relationships.

Symptoms are often grouped into three clusters. The first cluster contains so-called 'positive' symptoms, including delusions and hallucinations. These

are symptoms that are *not* present under normal circumstances. The second cluster contains 'negative' symptoms. These denote the absence of features, which normally speaking should be present. Examples of such symptoms are restricted range and intensity of emotional expression, reduced speech and thought productivity (alogia), anhedonia and decreased initiation of goal-directed behaviour (avolition).
The third cluster relates to 'disorganisation', for example, disorganised speech and chaotic behaviour.

Even today, the heterogeneity of the symptoms causes vehement debates about whether schizophrenia is just one syndrome or whether it is a cluster of related syndromes (Vlaminck 2002). Due to this lack of conceptual clarity during the last century different diagnostic procedures, each with its own diagnostic criteria, were used either simultaneously or in succession. During the last decade, the Diagnostic and Statistical Manual (DSM), which is published by the American Psychiatric Association (APA), has acquired a prominent position in the area of psychiatric diagnostics. The manual has now been issued for the fourth time (APA 1994) and there is a reasonable amount of consensus about the validity of the diagnostic criteria for schizophrenia. For a summary of the criteria, see table 1.

Schizophrenia: course

Schizophrenia usually manifests itself during adolescence or early adulthood. Men generally show symptoms a few years earlier than women (APA 1997). At the beginning of the twentieth century, the German psychiatrist Emil Kraepelin (1856-1926) – founding father of the classification of psychiatric disorders – described the illness 'dementia praecox', which later made its entry into the world of psychiatric nosology under the name 'schizophrenia'. Kraepelin assumed that schizophrenia was a degenerative disease leading, in the majority of cases, to serious psychiatric invalidity. According to Kraepelin, a mere 15% of patients showed any signs of recovery (in: Jablensky 1995). Subsequent studies show that the course and outcomes are more variable and that in a considerable number of patients - estimated to be between 25% and 45% - the illness develops relatively benignly (Bromet & Fennig 1999; Eaton 1985; Eaton 1991; Hegarty *et al.* 1994; Jablensky 1995; Ram *et al*. 1992; Wiersma *et al.* 1995). These patients experience one or more psychotic

Table 1 DSM - IV Criteria for Schizophrenia

A Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

- Delusions
- Hallucinations
- Disorganised speech (e.g. frequent derailment or incoherence)
- Grossly disorganised or catatonic behaviour
- Negative symptoms, i.e. affective flattening, alogia, or avolition

B Social/occupational dysfunctions: For a significant portion of time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C Duration: Continuous signs of the disturbance persist for at least six months. This 6-months period must include at least 1 month of symptoms (or less if successfully treated) that meet criterion A (i.e. active phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual symptoms, the signs of the disturbance may be manifested by only negative symptoms listed in criterion A present in attenuated form (e.g. odd beliefs, unusual perceptual experiences)

D Schizoaffective and Mood Disorder exclusion: Schizoaffective Disorder and Mood Disorder with Psychotic features have been ruled out either (1) no Major Depressive, Manic or Mixed Episodes have occurred during active phase symptoms; or (2) if mood episodes have occurred during active phase symptoms, their total duration has been brief relative to the active or residual periods.

E Substance/general medical condition exclusion: The disturbance is not due to the direct physiological effects of a disturbance (e.g. a drug of abuse, a medication) or a general medical condition

F Relationship to a Pervasive Developmental Disorder: if there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

episodes from which they recover relatively well. At the other end of the spectrum, there are between a quarter and a third of patients, who are seriously incapacitated by the illness. They depend on the care of others in their everyday lives. As for the intermediary group, which is estimated at between one-third and a half of the patient population, the course of the illness is characterised by relapses and a failure to make a full recovery. With the exception of periods of psychotic crises, these patients can lead a reasonably independent life, provided they receive sufficient support from others. It is estimated that 10% of patients commit suicide.

Interpreting the studies on the course of the illness is not without its problems. The diagnostic criteria for inclusion vary, as does the demographic composition of the cohorts. Furthermore, different criteria are used to typify the progression as 'good', 'moderate' or 'poor'. The duration of the studies can differ, which also affects the research outcomes. That over the last decade outcomes have been influenced by improved methods of treatment, including more effective antipsychotic medication, makes matters even more complicated. Moreover, more effective psychosocial interventions, which influence the course of the illness, have been developed and are used in treatment programmes for schizophrenic patients.

The level of premorbid functioning of schizophrenic patients is, in the case of between 25% and 50% of the patients, significantly below that of the population average (Buchanan & Carpenter 2000): their social adjustment is worse, they perform worse at school, they often lead a more isolated life and are emotionally less responsive. More often than not they suffer from cognitive impairments, including reduced attention and concentration levels. Subtle formal thought disorders are also often discernible in such patients. They often react to normal situations in an idiosyncratic manner. However, the premorbid features are highly non-specific, thus rendering them ineffective in terms of their prognostic value. They are of limited significance for early diagnosis.

Schizophrenia manifests itself with the appearance of psychotic symptoms. These symptoms appear gradually in about fifty percent of the patients and can be preceded by complaints lasting for months. In the other fifty percent of patients, the illness appears abruptly even though the patients have functioned normally up until that point. In such cases, a clear line of fracture is perceptible in the patient's personal history. For many patients, the

first five to ten years are marked by frequent relapses with or without complete remission. This period is followed by a phase of relative stability with less psychotic relapses. However, as already stated, a number of patients do not recover and remain chronically psychotic. Even if the positive symptoms decrease, the negative symptoms can still lead to serious social constraints.

Although the course of the illness cannot be determined in advance, there are a number of prognostic variables that are associated with good and poor prognosis (see table 2).

In addition to these prognostic variables, there are a number of factors that are known to specifically affect the re-occurrence of a psychotic relapse. In their literature review, Ayuso-Gutierrez & Rio Vega (1997) mention the following as the most important factors:

(1) Non-compliance with medication: non-compliance goes hand in hand with an increased risk of relapse.
(2) Medication strategy: the dosage, application method (oral or depot medication) and application strategy (continuous or intermittent) affect the risk of a relapse.
(3) Psychosocial factors: aggravating circumstances, such as stressful life-events or exposure to a social environment with a high level of expressed emotion, increase the risk of a relapse. In contrast, social support received from the patient's environment, and certain psychosocial interventions (family interventions, skills training and cognitive behavioural therapy) diminish the risk of a relapse.
(4) Alcohol and drugs abuse increase the risk of a relapse.

Table 2: Features Weighing Towards Good to Poor Prognosis in Schizophrenia	
Good Prognosis	Poor Prognosis
Late onset	Young onset
Obvious precipitating factors	No precipitating factors
Acute onset	Insidious onset
Good premorbid social, sexual and work histories	Poor premorbid social, sexual and work histories
Mood disorder symptoms (especially depressive disorders)	Withdrawn, autistic behaviour
Married	Single, divorced or widowed
Family history of mood disorders	Family history of schizophrenia
Good support systems	Poor support systems
Positive symptoms	Negative symptoms
	Neurological signs and symptoms
	History of perinatal trauma
	No remission in 3 years
	Many relapses
	History of assaultiveness

(Cancro & Lehmann 2000)

Psychotic Relapse

A psychosis is understood to mean a significant increase in the so-called 'positive' symptoms of schizophrenia. The most important of these symptoms are delusions, hallucinations and conceptual disorganisation (Kay *et al* 1987).

Delusions are ideas that are unrealistic and idiosyncratic. Hallucinations are sensory perceptions of auditory, visual, olfactory or somatic nature, which are not caused by external stimuli. Conceptual disorganisation is characterised by the interruption of purposeful sequences, for example, loose associations, drawing unwarranted conclusions and serious lack of logical reasoning.

Psychotic symptoms can lead to agitation and chaotic behaviour, and is sometimes accompanied with hostility towards people in the patient's surroundings.

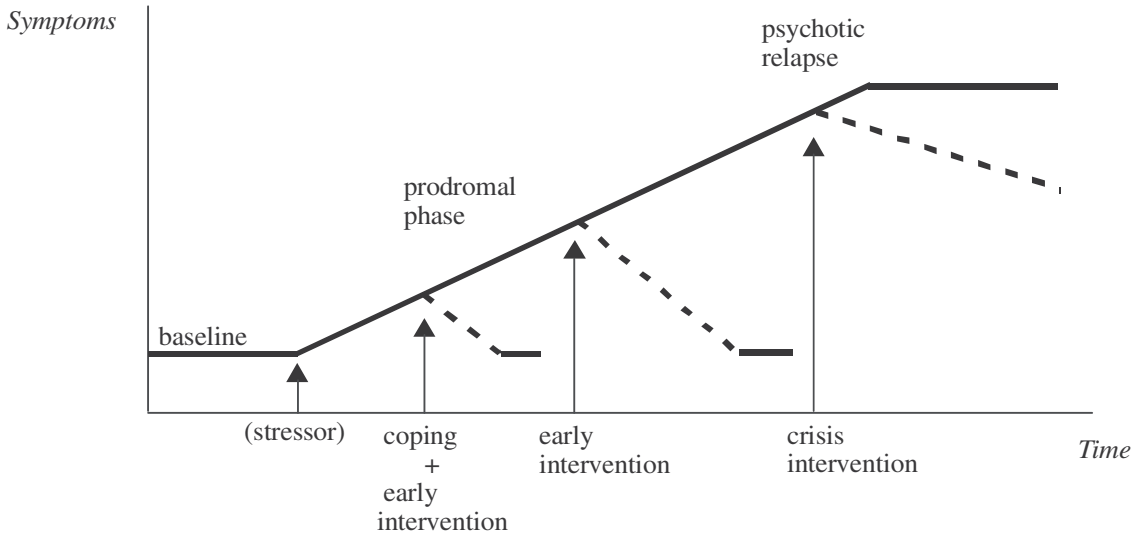

Figure 1: The process of psychotic relapse

It is obvious that in the case of the person quoted earlier (Lovejoy 1984) the psychosis developed very gradually. This gradual progression is also described in scientific literature. Herz & Melville (1980) demonstrated that in a large majority of the patients the phase preceding the onset of a psychosis - also called the prodromal phase - can last for several days, weeks or even months. This is an interesting observation in terms of prevention. Preventive action can be taken during this period in order to avert a psychotic crisis. The diagram in figure 1 illustrates the process of psychotic relapse.

The baseline indicates the level of symptoms, which a schizophrenic patient experiences on a more or less permanent basis. This level can differ considerably from patient to patient. After having a psychosis, one patient can be more or less free of symptoms, while another patient can be constantly plagued by persisting symptoms.

If symptoms increase slightly, relative to the baseline, many patients alter their behaviour in such a way as to ensure that the symptoms decrease or do not affect them so much. In the event that the symptoms get worse, the patient's ability to cope will not be sufficient and external intervention will be necessary. If intervention is made in the initial stage, it is known as 'early intervention'. If such early intervention is carried out effectively, it may encourage recovery, thus bringing the course of the illness back in the direction of the baseline. If the seriousness of the symptoms increases further, the result will be a psychotic crisis at some stage. In that case, it will be necessary to resort

will be a psychotic crisis at some stage. In that case, it will be necessary to resort to intensive interventions in the form of crisis management in order to deal with the crisis.

Strictly speaking, the changes at the beginning of the upward line cannot yet be regarded as symptoms (Bustillo *et al.* 1995). The symptoms are, for the most part, non-specific signs, which also frequently appear in the normal population. The fact that they appear in the phase preceding the onset of a psychosis makes them significant from a clinical point of view. In terms of semantics, it would be better to call them 'early signs'.

Definitions

With a view to providing conceptual clarity, a number of terms that are vital to understanding the following chapters are explained below:

The *prodromal phase* of psychosis is understood to mean the period lasting (mostly) between a few days and weeks prior to a psychotic relapse.

Early signs (*prodromes*) indicate changes in the perception, thought and/or behaviour of the patient. These signs appear in the prodromal phase of a psychosis and are, therefore, valuable tools for predicting a psychotic relapse.

Early recognition refers to the efforts that are made to recognise the early signs of a psychosis at the earliest stage possible.

Early intervention means that when the early signs of a psychosis become apparent, specific action is taken to prevent a serious psychotic crisis from developing. The aim of such action is to encourage the patient's balance to recover.

The intervention protocol for early detection and intervention, which is pivotal to this study, leads to a *Relapse Prevention Plan* being drawn up. This plan contains details of the early signs of a psychosis and the actions to be taken as part of the early intervention strategy.

Purpose and Relevance

The purpose of the research described in this thesis is twofold:

1. To develop an intervention protocol that may provide mental health nurses with support when drawing up a Relapse Prevention Plan aimed at preventing a psychotic relapse in schizophrenic patients;
2. To examine the effects of working with Relapse Prevention Plans in nursing practice.

Mental health nurses were chosen to perform the intervention because of the central role they play in the care of schizophrenic patients. In many cases, they are in frequent and prolonged contact with the patient and family members. This intense contact is an important prerequisite for performing an intervention, the aim of which is to constantly monitor the patient's clinical condition.

The significance of this research can be summed up in three points:

1. The percentage of relapses among patients suffering from schizophrenia and related disorders is unnecessarily high, given the current treatment conditions. The annual relapse rate is estimated to be around 40%. In optimum treatment conditions, this rate is between 15% and 20%. If extra efforts were made in the areas of pharmacological therapy and psychosocial interventions, the current level of relapses could be reduced further (see, among others, Ayuso-Gutierrez & Rio Vega 1997; Kissling 1991; Kissling 1992; Liberman & Kopelowicz 1995; Tarrier 1997; Viguera *et al*. 1997; Wirshing *et al.* 1991).
2. A psychosis almost always leads to a serious disruption of everyday life and future plans. In the majority of cases, the personal pressure under which the patient and his family are placed is tremendous. A psychosis can induce intense fears and can have traumatic consequences for the patient. From the point of view of easing the suffering of schizophrenic patients, prevention of psychoses should be given high priority (Baker 996; Bock 2000; Van den Bosch 1993; Levin & Daly 1998; Schene & Wijngaarden 1995; Shaw *et al.* 1997).
3. The costs to society of a psychotic relapse are very high. A considerable investment in people and resources is required for the treatment of a psychotic crisis and for the supervision of the patient during the recovery process. As a result, there is a growing demand for cost-effective

interventions, which may lead to a cutback in resources (APA 1997; Evers *et al.* 1995; Novacek & Raskin 1998; Rice 1999; Weiden & Olfson, 1995).

The above arguments have convinced various authors that prevention of psychotic relapse should be given the highest priority in the current treatment programmes (Masand & Berry 2000; Kissling & Leucht 1999; Kane 1999; Haro *et al*. 1998; Kane *et al.* 1998; Glazer, 1996; Glazer *et al.* 1996).

Structure of the Thesis

The study is built up as follows:
This introductory *Chapter 1* is followed by *Chapter 2*, which contains an overview of literature on early recognition and early intervention. In *Chapter 3* a general model for developing and testing nursing interventions will be presented. In the subsequent chapters, this model will be elaborated on for the main theme of this thesis, namely the development and testing of a nursing intervention protocol to be used for early recognition and early intervention. *Chapters 4* and *5* describe the results of an exploratory study into the already existing early recognition and early intervention practices in the Netherlands. The working procedures and the experiences of patients, family members and health care workers are examined. The results from Chapters 2, 4 and 5 provided the building blocks for the newly developed intervention protocol. *Chapter 6* describes the content of the intervention protocol for early recognition and early intervention. It also reports on the initial experiences from its use in nursing practice.

The results of a study on the effects of the intervention, carried out in three mental health care institutions, are presented in Chapters 7 and 8. *Chapter 7* examines the actual procedures and the experiences of mental health nurses who have applied the intervention protocol to one or more of the patients from their caseload. The data was obtained from a survey carried out among these nurses. *Chapter 8* describes the results of the experimental study into the effects of the intervention. Finally, *Chapter 9* generally discusses the results of the various studies of this thesis and the significance of the study as a whole

Chapter 2

Recognition of early warning signs in patients with schizophrenia:

A review of the literature

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- SUBMITTED -

Abstract

This article reviews and discusses the literature on the recognition of the early warning signs of psychosis in patients suffering from schizophrenia. The assumption is that nurses, in the everyday exercise of their profession, can contribute to the prevention of psychotic relapse in schizophrenic patients by the early recognition of warning signs of a psychosis. First of all, the process of psychotic relapse and the factors that influence it are described. Then, the research itself on the early signs is discussed. The article considers the questions of what the most common early signs are, when they occur, and who can recognize them.

The predictive value of the early signs is then considered: how well can psychotic relapse be predicted with these early signs? Finally, the research on the effects of early recognition and early intervention is discussed, primarily with respect to the question of whether psychotic relapses can actually be prevented by making use of preventive intervention strategies. The conclusion is that the preliminary results are hopeful and invite further research on such matters as the application of this intervention strategy within nursing practice.

Introduction

Schizophrenia is a serious psychiatric disorder with a life-time prevalence of approximately 0,8% (Buchanan & Carpenter 2000). The occurrence of psychotic relapse is characteristic of schizophrenia. Such symptoms occur as delusions, hallucinations, thought incoherency and seriously chaotic behaviour. The condition has a highly variable course with varying outcomes. In a considerable number of patients - estimated to be between 25% and 45% - the illness develops relatively benignly (Bromet & Fennig 1999; Eaton 1985; Eaton 1991; Hegarty *et al.* 1994; Jablensky 1995; Ram *et al*. 1992; Wiersma *et al.* 1995). These patients experience one or more psychotic episodes from which they make a relatively strong recovery. At the other end of the spectrum, there are between a quarter and a third of patients, who are left seriously incapacitated by the illness. They depend on the care of others in their everyday lives. As for the intermediary group, which is estimated at between one-third and a half of the patient population, the course of the illness is characterised by relapses and a failure to make a full recovery. With the exception of periods of psychotic crises, these patients can lead a reasonably independent life, provided they receive sufficient support from others.

Adequate medication therapy significantly reduces the risk of a psychotic relapse. As a supplement, psychosocial intervention is of great importance for influencing the disorder favourably. Supportive assistance of the patient and his or her family – with attention to information and education, therapy compliance, problem solving, and stress reduction – deserves a prominent place in care programs for schizophrenic patients. In addition, a number of skill and rehabilitation training programs have been proven to be effective, such as those directed to symptom and medication management, work, and living (Buchanan & Carpenter 2000; Bustillo *et al.* 2000; Marder *et al.* 1996; Wallace *et al.* 1992; Wirshing *et al.* 1991).

Much research has been done in recent years on the effects of medication and psychosocial interventions with the occurrence of psychotic relapses being the measure of outcome. Comparison of these studies on this measure of outcome is complicated by divergent operationalisations of psychotic relapse, differing research populations, and different treatment conditions (see, *inter alia*, Crow *et al.* 1986; Viguera *et al.* 1997; Kissling 1992; Gilbert *et al.* 1995; Shepherd *et al.* 1989; Ayuso-Gutierrez & Rio Vega 1997;

Liberman & Kopelowicz 1995; Linszen *et al.* 1996). Nevertheless, a pattern does emerge. Upon discontinuation of medication or with placebo treatment, very high relapse rates were found, in most studies between 60% and 75% after 1 year. Under favourable treatment conditions in which an optimal medication regime is offered (with intensive supervision of medication use) and intensive psychosocial assistance, rates were found of around 20%. Under regular treatment conditions, the relapse rate is estimated at about 40%. It must also be noted that studies with young patients show proportionally higher rates of relapse after their first admission than do those with chronic patients. Moreover, patients in a climate of high expressed emotion (EE) have a higher risk of psychotic relapse than do patients exposed to lower EE.

The importance of the prevention of psychoses is generally recognized (see, for example, APA 1997; Clinical Standards Board for Scotland 2002). A psychosis results in much personal suffering for the patient as well as for the people in his or her environment. Social recovery – insofar as this occurs – takes on an average one year (Hert & Slooff 2000). The treatment of psychotic patients costs a great deal (Evers *et al.* 1995; Rice 1999).

Focused measures with respect to psychosis prevention could reduce further the present relapse rates (Kissling 1991; Kissling 1992). One of the measures that has attracted interest in recent years is the early recognition of the warning signs of a psychotic relapse. The assumption is that these signs have a predictive value for the occurrence of psychotic relapses. Early recognition offers opportunities for early intervention, for example, in the form of medication adjustment, social support, and reduction of stress. In the early stages, these measures promote the recovery of equilibrium of the patient (Birchwood *et al.* 2000; Bustillo *et al.* 1995).

Relapse prevention by means of early recognition and early intervention is particularly relevant to nursing practice in view of the frequent and intensive contact that nurses maintain with schizophrenic patients. From this position, they can contribute to promotion of the self-management of the patient and of family caregivers. This contribution consists of monitoring the condition of the patient and the application of specific measures should the patient's condition require it. The further development and the testing of interventions in the area of early recognition and early intervention thus deserve a high priority.

In this review of the literature, we will compile an inventory of the knowledge about early recognition and early intervention directed to the prevention of psychoses in patients with schizophrenia. For this purpose, a

search of the literature was conducted in the Medline and Cinahl databases for the period from 1980 to 2002. The key words used were schizophrenia in combination with relapse, relapse prevention, prodrome, prodromal symptoms, early warning signs, early recognition and early intervention. Publications relevant to our subject were further sought on the basis of the reference lists of the articles found. The results of this search of the literature will be discussed in the light of their relevance to nursing practice.

The process of psychotic relapse

In this section, we will, by way of introduction, discuss the process of psychotic relapse and factors that influence it.

The vulnerability-stress-coping model is a commonly used theoretical framework for the research into, and the treatment of, schizophrenia (Zubin & Spring 1977; Zubin *et al.* 1992; Nuechterlein & Dawson 1984; Nuechterlein *et al.* 1992; Nuechterlein *et al.* 1994).

This model shows that various factors play a role in the development of a psychotic relapse. One factor is the vulnerability of the schizophrenic patient. This vulnerability is largely genetically determined and is present as a constant factor. Second, the amount of stress to which the patient is exposed is important. This stress can be caused by the patient himself or herself (for example, by means of all kinds of stress-inducing thoughts) or by environmental factors (for example, hostility on the part of people in his or her surroundings). A third factor are the coping and problem-solving skills of the patient. Most patients with schizophrenia do not submit to their situation passively but search for ways to deal with the aggravating circumstances. They also do this in the phase preceding the psychosis in which they perceive in themselves, disordering changes (Falloon 1987; Westacott 1995; Holmes *et al.* 1994; McCandless-Glimcher *et al.* 1986; Boker *et al.* 1989; Cohen & Berk 1985; Carr 1988; Baker 1995; Murphy & Moller 1993). The literature reports that patients have a very wide range of coping styles and that from them proceed several concrete coping strategies. The fourth factor in the vulnerability-stress-coping-model is the protection that the patient receives from his or her environment and that can serve as a buffer against stress. The protection can consist of practical, emotional, and social support to enable the patient to better handle the consequences of the illness (Wing 1978).

The complex interaction between vulnerability, stress, coping, and protection determines whether a patient psychotically decompensates at a given moment. It also determines the gravity of the relapse. When the first signs of a psychosis become apparent, one can act on the various factors of the model in order to counter the aggravation of the psychosis, such as by increasing medication, reducing stress, promoting coping, and taking protective measures in the environment.

Docherty *et al.* (1978), on the basis of a review of case studies and phenomenological studies, have tried to describe the process of psychotic relapse in six phases. In Phase 0, there is an equilibrium condition in which the patient functions well and succeeds in adapting relatively well to the demands the environment places on him or her. In Phase 1 (overextension), cognitive overload occurs accompanied by symptoms of anxiety, irritation, distractibility, and reduced performance. In the phase that follows, Phase 2, the patient experiences restricted consciousness. Apathy, listlessness, social withdrawal behaviour, feelings of hopelessness, loneliness, boredom, and dependence are some of the phenomena that often occur in this phase. In Phase 3, disinhibition, phenomena can occur that point to disturbed impulse regulation, such as sexual disinhibition, anger attacks, and excessive spending of money. In this phase, the mood may also be seen to improve. In Phase 4, psychotic disorganization occurs together with perceptual and cognitive deterioration, ultimately leading to total fragmentation of the consciousness and loss of self-control. In the last phase that Docherty *et al.* describe, reorganization of the psychotic consciousness occurs, for example in the form of a paranoid delusional system. This leads to the recovery of control and reduction of anxiety (psychotic resolution).

The description of Docherty *et al.* is interesting for our present purposes because they were the first to have tried to introduce some structure into the complex process of psychotic relapse. Many of the phenomena cited were also described as early warning signs in later research (see the next section). The authors describe how a number of phenomena can be seen as coping strategies for incipient psychotic symptoms.

This structuring also gave rise to criticism (see, for example, Vries & Delespaul 1988). The process description would not do justice to the dynamics between the various factors of the vulnerability-stress-coping model. According to the critics, the process is presented too deterministically and

pessimistically, and justice is not done to the variability between patients. Such a prototypical course of psychotic relapse does not exist.

Birchwood and Spencer (2001) present a simpler model in which three phases are distinguished. In the first phase of relapse, primarily cognitive-perceptual changes occur, such as attentional dysfunction, derealisation, and racing thoughts. They progress to phenomena of dysphoria, accompanied by a depressive mood, pre-occupation with mental life, and loss of interest and self-care. In the third phase, the pre-psychotic or psychotic symptoms emerge to a greater extent, including suspiciousness, ideas of reference and mild hallucinations.

In the literature, the question is raised about when one can still speak of early warning signs and when there are clear psychotic symptoms. According to Norman and Malla (1995), it is important to make a clear conceptual distinction between early signs and psychotic symptoms. However, this transition proceeds gradually and the introduction of a cut-off point is always arbitrary (Tarrier *et al.* 1991). For everyday practice, this distinction does not seem to be particularly important. Indeed, it is a matter primarily of reacting in as early a stage as possible to changes in the condition of the patient that point to an impending psychotic relapse (see also Bustillo *et al.* 1995). In the next section, we will go further into the nature of the early warning signs.

Early Warning Signs

Early warning signs of a psychosis can be defined as subjective experiences, thoughts, and behaviours of the patient that occur in the phase preceding a psychotic relapse (Heinrichs & Carpenter 1985; Herz & Melville 1980). The question is now which experiences, thoughts, and behaviours are characteristic for this phase.

Heinrichs and Carpenter (1985) conducted a prospective study of the early warning signs of a psychosis in 47 ambulatory patients with schizophrenia (n=38) or a schizoaffective disorder (n=9). During weekly appointments with the client, clinicians noted whether or not warning signs were present that indicated an impending psychotic relapse. On the basis of this, 32 early warning signs were identified. The ten most common are: hallucinations (53%), suspiciousness (43%), change in sleep (43%), anxiety

(38%), cognitive inefficiency (26%), anger/hostility (23%), somatic symptoms or delusions (21%), thought disorder (17%) disruptive inappropriate behaviour (17%), and depression (17%).

When we look at the cumulative frequencies, then it is striking that all of the patients manifested at least one of these symptoms. The summary shows a mix of psychotic and non-psychotic symptoms, in which it is striking that the psychotic symptoms score high in comparison to the non-psychotic symptoms. This contrast with the retrospective study of Herz and Melville (1980) whereby the non-psychotic warning signs – observed by patients and family members – score much higher in the ranking. Apparently, it makes a difference whether the warning signs are registered prospectively or retrospectively and also who does the registration. It is possible that symptoms of dysphoria are indeed present, but are reported less by the patient and are also less directly observed by the care provider. They occur more in the experience of the patient and are not always expressed in concrete behavioural terms. When they are observed, then there is still the question of whether they are interpreted as warning signs of a psychosis. It could be that they are more apt to be attributed to the psychosis afterwards than at the time they occur.

Many of the early warning signs that are cited in other literature sources match those cited above or can be seen as explicit behavioural expressions related to these symptoms. The descriptions show that, even though certain early warning signs occur relatively frequently, individual variation is very great ((Heinrichs & Carpenter 1985; Herz & Melville 1980; O'Connor 1991; Tarrier *et al.* 1991; Kumar *et al.* 1989; Hamera *et al.* 1992; Subotnik & Nuechterlein 1988; Kennedy *et al.* 2000).

One much used scale for the measurement of early warning signs is the Early Signs Scale developed by Birchwood *et al.* (1989). This scale has satisfactory psychometric characteristics. The authors classify the most common early warning signs in four subscales: (1) anxiety / agitation, (2) depression / withdrawal, (3) disinhibition, and (4) incipient psychosis. The warning signs of the first two subscales occur primarily in the dysphoria phase. The warning signs of the last two subscales are visible primarily when the process of relapse has progressed further and the experiences and behaviours gradually take on a more psychotic character.

Alongside the more general early warning signs, as described above, the so-called idiosyncratic behaviours are also of importance for the early recognition of a psychosis (Norman & Malla 1995; Herz & Lamberti 1995;

Bustillo *et al.* 1995; Campo & Merckelbach 1996). These are very eccentric behaviours of the patient that often constitute an unmistakable signal for those in his or her environment that the condition of the patient is deteriorating. For example, the patient puts on striking clothing, dyes his or her hair in a striking colour, conducts certain magic rituals, or becomes engrossed in mathematical problems (without having a talent for it). A number of authors stress the importance of preparing a "relapse signature" for each patient that includes both the general early warning signs and the specific idiosyncratic behaviours (Birchwood 1992; Birchwood *et al.* 1992).

Recognition of early warning signs

For the use of early recognition and early intervention in care practice, two conditions need to be met: patients and the people in his or her environment must be able to recognize the early warning signs of a psychosis; and there must be sufficient time between the moment of the occurrence of the first warning signs and the time of serious psychotic relapse in order to make early intervention possible. We will now discuss these two conditions.

Herz and Melville (1980) conducted a retrospective study in which they interviewed 145 patients and 80 family members. The patient group consisted of stabilized patients who were being treated on an ambulatory basis (n=99) and partially of clinical patients who were recovering from a psychosis (n=46). The respondents were asked if they could indicate changes in experiences, thoughts, and/or behaviours that preceded the most recent psychotic episode. The conclusion was that 70% of the patients and 93% of the family members could name one or more specific changes. There was great agreement between patients and family members about the most important warning signs (Spearman rank-order correlation = .78 / $p < .001$). The least agreement was about the pre-psychotic or psychotic symptoms, such as incoherent speech and visual hallucinations. The family members scored them higher than did the patients. The authors state that this was probably due to denial on the part of the patients of psychotic symptoms.

In a retrospective study by Kumar *et al*. (1989) on the recognition of early warning signs and the coping strategies that followed, 86% of de patients could name one or more signs. Heinrichs *et al.* (1985) found a lower percentage of 63%.

A limitation of retrospective studies is that patients may well be able to name the warning signs of a psychosis when looking back, but this does not guarantee recognition and acknowledgement when they actually occur.

Patients can play down the changes in their condition at the time they occur because of their desire to function healthily. The ability to recognize symptoms (and to attribute to them their correct significance) can also diminish as the process of relapse progresses because the degree of illness insight decreases (Birchwood *et al.* 1992; David 1990; McEvoy *et al.* 1989; Van Meijel & Lendemeijer 1997). The literature is not clear about the number of patients in whom this problem occurs or the degree of gravity with which it occurs.

For the time being, it may be concluded that adequate recognition of early warning signs is improved by involving several parties: the patient himself or herself, the family or other members of the social network, and the care providers. When the recognition capacity of the patient diminishes, others can take over this task. Family members in particular are well able to notice subtle changes in the patient, so they can make an essential contribution to the monitoring of the condition of the patient (Carpenter & Heinrichs 1983).

The question of the period between the first warning signs and the psychotic relapse is particularly important from a clinical perspective. One condition for effective early intervention is that this period be of sufficient length. The research results are hopeful in this regard. The study of Herz and Melville (1980) shows that this period was reported by patients and family members to be less than one day in only a few cases (7 - 11%), in which there was hardly time to intervene. A larger percentage (16-24%) said that this period lasted from one to seven days, but a majority of the patients and family members (50 - 68%) reported a period of more than 7 days extending to longer than a month.

Other retrospective and prospective studies confirm that an increase of early warning signs and/or symptoms is apparent for several weeks before a psychotic relapse in a majority of cases (Subotnik & Nuechterlein 1988; Tarrier *et al.* 1991; Birchwood *et al.* 1989; Henmi 1993; Birchwood *et al.* 1992).

The conclusion is that, in a great majority of cases, the time interval between the first early warning signs and serious psychosis is long enough to give sufficient opportunity to apply early intervention strategies. With a small

minority – probably less than 10% – the psychosis occurs so rapidly that preventive measures have little or no chance of succeeding.

Predictive value

The significance of early recognition and early intervention increases with the increase of the predictive value of the warning signs for the occurrence of a psychotic relapse. There is still relatively little knowledge about the question of which early warning signs are good predictors of a psychotic relapse. Malla and Norman (1994), Tarrier *et al.* (1991) and Hirsch and Jolley (1989) consider the occurrence of depressive feelings to be a good predictor. Other authors point primarily to the high predictive value of mild psychotic phenomena (Birchwood 1992; O'Connor 1991; Tarrier *et al.* 1991; Jorgensen 1998).

For the evaluation of the clinical and conceptual significance of early warning signs, one needs a prospective analysis of the relationship between warning signs and psychotic relapse (Malla & Norman 1994). The positive predictive value (PPV) can then be measured, that is, the probability that observed early warning signs will actually be followed by a psychotic relapse. One problem here, however, is that, in clinical practice, one generally intervenes therapeutically upon the occurrence of warning signs of a psychosis, so the natural course of symptom development is interrupted. The chance of a psychotic relapse is reduced upon successful intervention. When a psychotic relapse would have occurred under natural circumstances, it is prevented by therapeutic intervention. With this, the PPV of the early warning signs declines. No alternatives are conceivable for the determination of this predictive measure because, for ethical reasons, therapeutic intervention is, in principle, always indicated when it is established that the condition of the patient deteriorates.

The PPV has been determined in three studies, and also in these studies pharmacological and psychosocial interventions affected the natural course of the symptom development resulting in low or very low PPVs ranging between 15% to 43% (Marder *et al.* 1994; Gaebel *et al.* 1993; Jolley *et al.* 1990). These studies confirm that the most active interventions do indeed lead to the lowest PPV.

Most researchers concentrate on establishing the sensitivity and the specificity of early warning signs (Subotnik & Nuechterlein 1988; Hirsch & Jolley 1989; Jolley *et al.* 1990; Birchwood *et al.* 1989; Tarrier *et al.* 1991; Marder *et al.* 1994; Marder *et al.* 1991; Gaebel *et al.* 1993; Jorgensen 1998; Malla & Norman 1994).

Sensitivity refers to the proportion of relapsing patients for whom there was an earlier increase in early warning signs (true positive rate), whereas specificity refers to the proportion of *non*relapsing patients for whom there was *no* increase in early warning signs (true negative rate). Here, too, one must note that therapeutic interventions affected the research results.

As regards the sensitivity of early warning signs, no consistent picture has emerged: the sensitivity varies in the various studies between 8% (Gaebel *et al.* 1993) and 81% (Jorgensen 1998). Most of the studies score well above 50%. For the specificity of the early warning signs, a somewhat more univocal picture emerges: the values lie between 60 and 93%.

Further examination of these studies shows that the degree of comparability is very small. Differences in practical and methodological choices account for a part of the variable outcomes. We list the most important of them.

The first important factor is the selection of the early warning signs of which the predictive value is established. For example, Gaebel *et al.* 1993 selected six common early warning signs and conducted a prospective study of their predictive value within different treatment conditions. The pre-selection, based on the research of Herz and Melville (1980), consists of a number of non-specific symptoms and symptoms of dysphoria. The sensitivity did not exceed 14%. Jorgensen (1998), however, used the 34-item Early Signs Scale (Birchwood *et al.* 1989) in which pre-psychotic symptoms are also included that are known to have a greater predictive capacity. This scale was filled in by the patient himself or herself. The authors arrived at a sensitivity of 74% in their study. One may conclude in this regard that differences in the pre-selection of the early warning signs that are used in the study contribute to the differences in the predictive outcome measures found. Therefore, the conclusion of Gaebel *et al.* (1993) that the clinical significance of early warning signs is limited because of the low predictive value is, in our opinion, very premature.

A second problem is that the early warning signs are scored with varying frequencies in the studies, sometimes once in four weeks. This last

frequency is certainly too low, since a large portion of the psychotic relapses arises within a few days or weeks. With low frequency scoring, early warning signs that are indeed present will not be noticed in some of the patients, which leads to the incorrect conclusion that no warning signs preceded the psychosis. The possibility of preventive intervention is reduced sharply with such low frequency monitoring.

Third, the studies apply different operationalisations of psychotic relapse, which affects the predictive values that are found.

Fourth, the follow-up-periods vary considerably in the studies, which makes it difficult to compare the outcomes.

Because of these problems – and particularly because of their combination the study of the predictive value of early warning signs provides little clarity. It is important to conduct further research into the conditions under which satisfactory predictive values can be achieved. Low sensitivity of early warning signs is certainly a problem for clinical practice, for it means that a large portion of the psychotic relapses are not preceded by early warning signs, which correspondingly reduces the importance of early recognition. A low specificity score would also be a problem for it would mean that many patients who do not have a psychosis but who do show early warning signs are given unnecessary treatment and undergo the accompanying stress.

The question is now how can the predictive value of early warning signs be optimised within clinical practice. It is important to prepare an individual profile, a "relapse signature", for each patient on the basis of previous psychotic relapses of early warning signs in which the pre-psychotic warning signs, along with the more aspecific symptoms have a place (Birchwood 1992; Birchwood *et al.* 1992). Using standard instruments can be helpful, but it must not be forgotten that certain warning signs are highly idiosyncratic and therefore do not appear on the standard lists. An open clinical interview with the patient and with family members is indicated to identify these idiosyncratic symptoms.

Research on the effects

Research on the effects of early recognition and early intervention is scarce. Most of the research has been done on the application of early recognition methods combined with divergent medication strategies (Gaebel

et al. 1993; Gaebel *et al.* 2002; Herz *et al.* 1991; Herz *et al.* 1989; Herz *et al.* 1982; Marder *et al.* 1994; Carpenter *et al.* 1990; Schooler *et al.* 1997; Schooler *et al.* 1995; Inderbitzin *et al.* 1994; Pietzcker *et al.* 1993; Jolley *et al.* 1990).

Generally, it concerns the comparison of maintenance medication in variable dosages with intermittent strategies with which anti-psychotic medication is administered upon the first signs of an approaching relapse. Systematic monitoring of early warning signs is part of the intermittent medication strategy. The occurrence of psychotic relapse is the primary outcome measure in these studies.

A detailed description of the results of these studies goes beyond the scope of this article. The data relevant to our purpose can be summarized as follows.

Intermittent medication strategies appear in general to be inferior to the strategies of offering maintenance medication, also when the intermittent medication policy is combined with intensive monitoring of early warning signs. Intermittent medication strategies lead to less medication consumption and fewer side effects such as tardive dyskinesia, extra-pyramidal symptoms, and negative symptoms caused by neuroleptica. These side effects are often very burdensome for the patient and hinder personal and social functioning. They have a negative impact on medication compliance. The benefits from reduced side effects achieved by the intermittent medication strategy, however, is overshadowed by a higher risk of relapse, so most authors advise against it or propose stringent selection of the patients for whom this strategy could be indicated. Maintenance medication still seems to be the best way to prevent psychoses.

The conclusion is that early recognition and early intervention are recommended mainly in combination with medication maintenance treatment and cannot serve to replace this treatment. Early recognition and early intervention of themselves have an added value with respect to maintenance medication. Adequate early recognition can lead to an early increase of the antipsychotic medication and thus have a preventive effect.

The studies cited above always combined different medication interventions with the application of early recognition and early intervention. In order to establish the effectiveness of early recognition and early intervention as such, it is necessary to standardize the medication treatment. Two studies are important here.

Herz *et al.* (2000) conducted a controlled study on the effects of a program for relapse prevention in schizophrenia. The experimental group received a combination of (1) psychoeducation about psychotic relapse and early warning signs, (2) active monitoring of early signs, (3) early intervention upon the occurrence of early signs, (4) supportive group or individual meetings directed to improving coping skills, and (5) multifamily psychoeducation groups. The patients in the control group were offered care as usual consisting of individual supportive therapy and medication management. The patients of both groups were prescribed standard doses of maintenance medication. During the follow-up period of 18 months, the patients in the experimental group had significantly fewer psychoses than did the patients in the control group (17% vs. 34%) and were readmitted less often (22% vs. 39%).

Stenberg *et al.* (1998) studied the effects of the Liberman Module 'Symptom Management' with readmission as the outcome measure. This is a group-education program focusing on early recognition and early intervention. The control group received care as usual. The follow-up period was 2 years. The researchers concluded that the number of readmissions did not differ between the experimental and the control condition but that large differences did occur in the duration of the hospital admissions. The experimental patients stayed an average of 2.6 weeks in the hospital while the control patients stayed 20 weeks. This indicates that the patients who had participated in the training program had had much less serious psychoses than did the patients in the control group.

Indicative of possible effects is also the descriptive correlational study of Novacek and Raskin (1998) of 370 ambulatory patients with a serious psychiatric disorder. A good half of the patients suffered from schizophrenia. Data on a large number of areas – including the area of early recognition and illness course – were compiled with the aid of score lists filled in by case managers, interviews with patients, and client-service records. The research results indicate that poor recognition of warning signs was related to poorer treatment outcomes and greater use of expensive types of services. Improvement of recognition was related to better treatment outcomes and lower costs.

The effects of early recognition and early intervention can also be defined in terms of changed experience of the illness. Research into illness experience – and the way in which this is influenced by self-management strategies – has hardly been developed. The hypothetical statements of various authors arise mostly from experience. The application of early recognition and early

intervention would lead to increased self-efficacy of the patient as regards the self-management of the illness and the exercise of control over his or her own life. This would lead to enhanced self-respect of the patient (see, for example, Carpenter & Heinrichs 1983; Breier & Strauss 1983). The research of Boevink *et al.* (1995) into the quality of life of chronic psychiatric patients demonstrates the importance for psychiatric patients to get hold of their own life, to have a perspective to the future, and to learn to deal with themselves and their mental problems adequately. Further research is desirable in this area.

Discussion

Because of the disorder that serious psychotic relapse can cause in the life of the patient and his or her family, high priority must be given to its prevention. Our hypothesis is that a more systematic application of early recognition and early intervention strategies in nursing practice can contribute to this objective and thus provide health benefits for the patient.

On the basis of the literature discussed, there is sufficient reason to state that early warning signs generally precede a psychosis. Adequate recognition of these signs makes early intervention possible. There is also a moderate degree of optimism justified about the effectiveness of early recognition and early intervention for the prevention of psychotic relapses, but the research is still scarce and the conclusions are very provisional.

The development and testing of interventions in the area of early recognition and early intervention must be a priority. In a number of the studies discussed – particularly in the medication studies – the methods of early recognition applied are very rudimentary, for example consisting of one or a few educational meetings with patients and possibly family members in which information was given about early warning signs and their significance for the prevention of psychoses. Among others, Jolley *et al.* (1990) add on critical comments. The methods of early recognition and early intervention need further development, and their implementation in care practice must be done in a structured manner. Early recognition and early intervention are not activities to be conducted for a specific period of time but rather continuously and require a structural imbedding within the helping relationship.

At present, group education programs are already available for medication and symptom management, having been developed by Robert Paul Liberman and his colleagues at the University of California. For nursing

practice, however, there seems also to be a need for methods that are tuned more to the individual helping relationship with the patient and the family in which account can be taken of patient-related and contextual characteristics. This need appears from the initiatives that spontaneously developed within mental health care organizations in the Netherlands to develop these methods. A scientific foundation is needed for them, as appeared from a field inventory that was compiled in the Netherlands of existing early recognition and early intervention practices (Mierlo 1997).

The authors of this article have conducted a qualitative study of present intervention practices in the area of early recognition and early intervention in the Netherlands (Van Meijel *et al.* 2002b; Van Meijel *et al.* 2002c). This study led to an understanding of the routines and methods used. An understanding was acquired also of the experiences of care providers, patients, and family members with the application of these routines and methods. Thus, the factors emerged that promote or hinder effective execution of methods of early recognition and early intervention.

On the basis of the literature data and the results of the qualitative study, a nursing intervention protocol was developed that has the objective of providing an individualized application of early recognition and early intervention. This is tuned to the characteristics of the patient and of the social network. The expectation is that this will have a positive impact on the effectiveness of the intervention. The individualizing intervention strategy can be offered in conjunction with group education, but it can also replace it, for example when the patient cannot or does not want to participate in a group-education program.

Chapter 3

The development of evidence based nursing interventions:

Methodological considerations

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- SUBMITTED -

Abstract

The call for Evidence Based Practice (EBP) presents numerous challenges to nurses who are responsible for developing interventions and expanding the associated knowledge base. EBP is often associated with the assumption that Randomised Controlled Trials (RCT) are the most evident means to establish the value of an intervention. Scant attention however, is given to the limitations of RCTs. Furthermore, limited literature concerning development of evidence based nursing interventions is available. The authors describe a model to develop and test complex nursing interventions. The model is appropriate for interventions in which the experience of the client plays an important role. The model consists of four stages: Problem Definition, Accumulation of Building Blocks for Intervention Design, Intervention Design and Intervention Validation. In this article each stage is described and examples from research studies are presented. Specific attention is given to the manner in which the model allows for the accumulation of empirical evidence and theory development during the development process.

Introduction

Nursing science and the nursing profession have given considerable attention to the validation and empirical testing of clinical interventions. The call for Evidence Based Practice (EBP) that medicine and other (health) disciplines share, has only increased this interest. Since EBP has come on the scene, Randomised Controlled Trials (RCTs) are thought of as the evident means to establish the value of an intervention. Limitations of RCTs are given only scant attention. Moreover, the development of interventions, as opposed to their testing, is rarely discussed. In this article, a contribution is made to the limited literature concerning development of nursing interventions and a discourse is initiated concerning empirical methods used in the development process. First, the limitations of RCTs in establishing the validity of nursing or clinical interventions are briefly discussed. Then the process of developing and testing new interventions that is used in the Nursing Science Department at the Utrecht University (The Netherlands) is presented.

Limitations of RCTs

Epidemiologists, and others who espouse EBP, consider RCTs the strongest evidence for the validity of interventions. However, RCTs have serious limitations when developing knowledge for use in nursing practice is concerned.

RCTs in nursing, and often also in medicine, do not provide evidence for general laws, but allow only probabilistic conclusions. The RCT does not demonstrate that something is true for any given case, but for a general number of cases. When, for example, an RCT demonstrates that it is beneficial for children to have their parents present during a threatening procedure, this

will not be the case for all children. Children who have experiences that differ from the mainstream (for example: abused children or children who are often punished for crying) may not benefit at all. RCTs seldom bring these limitations to the surface. Consequently nurses, who want to use “effective interventions”, lack the information they need in order to decide whether or not to apply an intervention in a particular situation.

RCTs do not really allow testing variations in the intervention. Even when a factorial design is used, it is impossible to test all the decisions that must be made about how to mould the intervention. For example, in a study about follow-up care of gynaecological cancer patients the choice had to be made whether to invite only the women concerned, to also invite their partners, or to let the women choose. Researchers (or the clinicians who advise them) often make arbitrary decisions because evidence is not available. Consequently sub-optimal forms of the intervention may be tested in the RCT.

Sample issues may further limit the validity of the results of an RCT. Interventions usually have limited generalisability. For example, an intervention may be beneficial to some types of patients with schizophrenia and not to others. This becomes apparent only if subgroup analysis is conducted. Subgroup analysis, however, is only possible if the number of subjects in the subgroup is sufficiently large and the variables that may affect the outcomes associated with the intervention are conceptualised and measured. Without adequate attention to subgroup analysis, the RCT may lead to false positive or, more often, false negative conclusions.

RCTs provide evidence about the effects of an intervention. However, they do not provide insight into the reasons why an intervention is effective. If the intervention is not based on theory and no empirical evidence is offered, then it is impossible to predict which actions or aspects of the intervention are essential for its effect and which ones are subsidiary or of no importance. This information is indispensable to the clinician. Indeed, without the information, the clinician has no choice but to apply the intervention exactly as tested in the RCT. Yet this is often impossible, since the work situation of the clinician is seldom exactly the same as in the trial. If the clinician adapts the intervention to better suit the situation, then the aspects that are necessary for the effect may be omitted because the clinician is forced to base judgments on assumption rather than on evidence, which is lacking.

Evidence based nursing practice is the use of empirical research findings to achieve a higher reliability in successfully achieving the desired results. Such practice depends on more than the results of RCTs. Also indispensable is insight into the processes that are responsible for the results as well as understanding the limitations of a successful intervention. Our assertion is that qualitative research used in the development of clinical interventions plays a vital role in complementing RCTs. In the subsequent

section, a method of developing certain types of clinical interventions consistent with this assertion is presented.

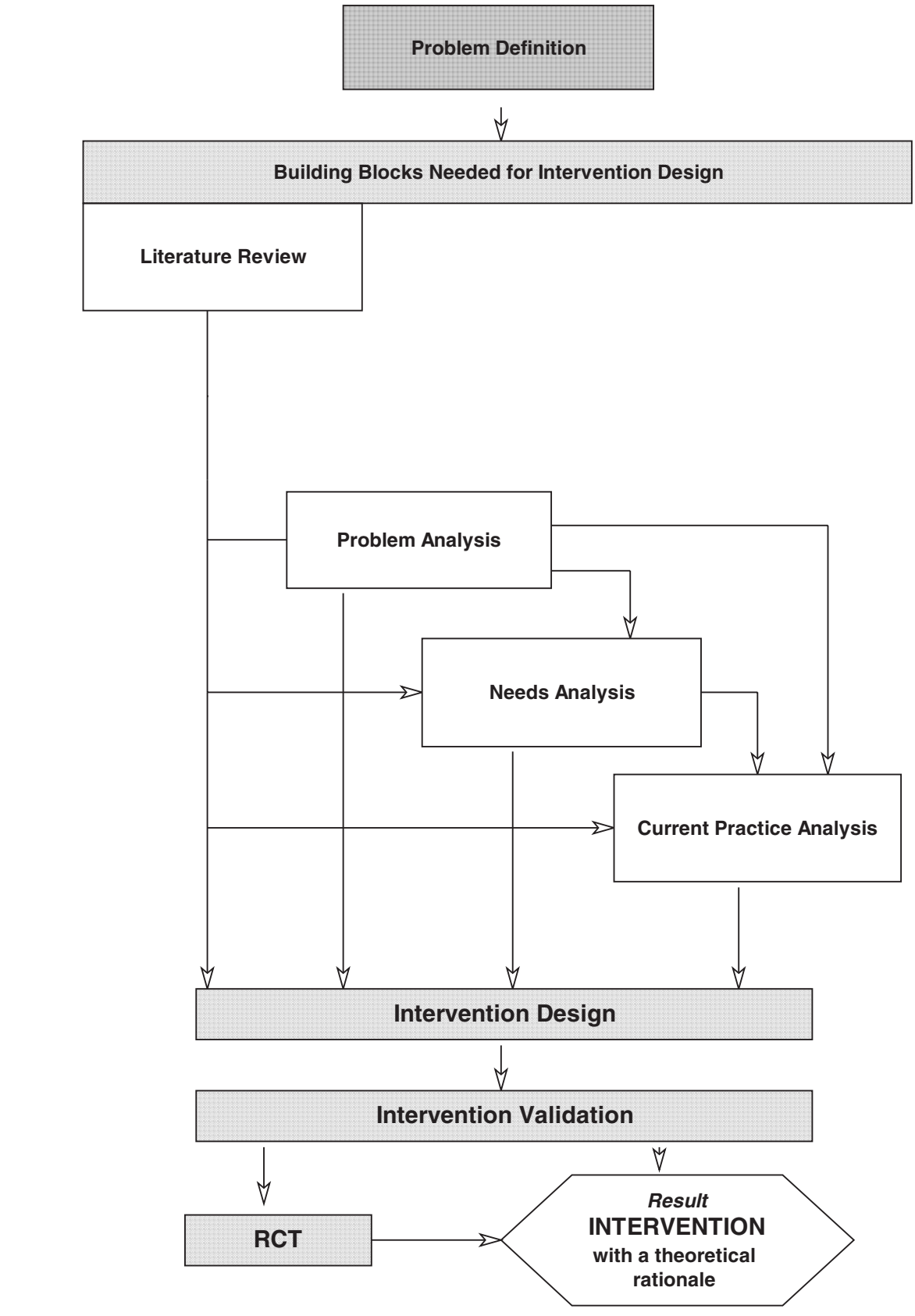
Core issues of intervention development

The basic model for developing evidence based nursing interventions that was formulated and is used by the Nursing Science Department at the Utrecht University, is presented in Figure 1. The model consists of four stages: Problem Definition, Accumulation of Building Blocks for Intervention Design, Intervention Design and Intervention Validation. During the Accumulation of Building Blocks stage, a Literature Review is a required step. Problem Analysis, Needs Analysis and Current Practice Analysis may or may not be necessary. The decision to include one or more of these steps and the selected strategies depend upon, among other things, the nature of the problem that the intervention aims to alter, the nature of the intervention and the state of knowledge concerning the intervention and related subject areas. The nature of the interventions that is examined in this article can best be described as complex and composite interventions in which the experience of the client[1] plays an important role. This experience can play a role in two ways, first as a process variable while carrying out the intervention and second as an outcome of the intervention. In this section of the article, the general aspects of the development process are presented. In subsequent sections, each stage is further developed.

The goal of the first stage is to formulate a work definition of the problem that is the focus of the intervention. This definition forms the basis for the second stage, during which building blocks needed to design an intervention are accumulated. An essential strategy is a thorough review of the literature. The full depth of the problem as well as the intervention area is studied. The degree to which theories and or models for the intervention area (or related fields) are available for use in directing the development process is determined. The state of knowledge and the experience in using similar interventions in clinical practice establish the course of development, refinement and testing that is followed. Numerous variations in the course are possible. Based upon the findings of the literature review, one or more of

[1] In this article client refers to the patient, family and informal care-giver

Figure 1 : Diagram of Developing Evidence Based Interventions



the following additional strategies may be deemed necessary: Problem Analysis, Needs Analysis and Current Practice Analysis

During the Literature Review, first the question needs to be answered, how clear the nature is of the problem that the intervention aims to alter. In other words, what exactly is the problem and what are the experiences of clients and caregivers with this problem? When the nature of the problem is unclear, then the first priority is further Problem Analysis in order to realise a solid connection between the problem and the content of the intervention.

The second question that deserves attention is, what type of (nursing) care can contribute to resolving, reducing or altering the problem. In order to answer this question adequately, knowledge concerning the need for care from the perspective of the client is essential in addition to professional knowledge. The degree to which the intervention meets clients' needs and is congruent with their experiences are important criteria for the evaluation of the success and effect of the developed intervention. If the experience or perspective of the client is missing or incomplete in the reviewed literature, then further research in the form of a Needs Analysis is indicated.

The third question that is addressed during the literature review concerns the availability of nursing interventions or useable interventions from other disciplines. The available interventions are closely scrutinised to determine the manner in which they were developed, the established effectiveness, the acceptability of the intervention for the client and the feasibility of use by nurses. If limited or no research is found, then a study of the experience with currently used interventions may contribute valuable insight (Current Practice Analysis).

The answers to the previous questions provide the building blocks for further intervention development. Using the existing literature and research findings, a first draft of the intervention is written. Because complex and composite interventions are the focus of this development process, attention is given to the diverse actions associated with the intervention. A rationale for the actions, based on the available research and theory, is formulated. Experts in the intervention domain give their opinion and contribute, in this manner, to this stage of the development process.

The final stage of intervention development commences once the first draft of the intervention is formulated. During the stage of Intervention Validation, the preliminary form of the intervention is used and studied in

nursing practice. The case-study method is especially suited for this purpose because it allows for evaluation of the diverse components of the intervention. Experiences and results associated with the components are systematically evaluated using qualitative methods. Based upon the findings, the intervention is modified as needed.

Once the definite form of the intervention is validated, the decision is made to either conduct effect research or to proceed with implementation research.

Throughout all stages and wherever relevant, the contribution of the chosen strategy and findings to theory development related to the intervention are conceptualised and described.
In what follows each of the phases will be discussed in greater detail.

Problem Definition

The existence of a problematic situation is usually discovered through direct signals from nursing practice. Another source is the perspective of the client who experiences a problematic situation for which a (satisfactory) solution, at that time, is not available. Additionally, previous research and theory are important stimuli that lead to the identification of problem situations that need to be resolved through new research. Insight from the client, nursing and theory perspective are used to formulate a work definition of the problem. A few examples from our studies follow:

- *Many patients and their partners want information concerning the influence of gynaecological cancer on sexuality. Nurses are in the position to provide information and offer support as part of their daily practice. Yet literature search reveals no tested interventions for the promotion of sexual adaptation and the prevention of sexual problems. The reviewed literature, however, contains numerous suggestions that can be used to formulate recommendations for intervention development (Gamel et al. 2001).*
- *Parental participation in the care of chronically ill children is an important issue for paediatric nurses. Literature review confirms this practice observation. Theory based guidelines for parental participation however are not available. Each nurse tends to carry out parental participation in her own way and that is not always*

consistent with the wishes of the parent. Consequently, guidelines for working with parental participation are needed (Van Swieten-Duijffjes 1998).

- *Many patients who suffer from schizophrenia have repeated psychotic relapses. Theoretical knowledge concerning the factors that increase the risk of psychotic relapses is available. Moreover, the process of psychotic decompensation, from the very first signs until the moment of a serious psychotic crisis, is well known. The question is how can nurses effectively contribute to early recognition of a psychotic relapse, so that intervention can begin as early as possible? (Van Meijel 1996).*

The initial exploration of the problem and formulation of the work definition require a careful approach. The problem definition needs to be formulated in a way that gives direction to the review of the literature. The limitations are established and a distinction from similar problems is made. As the boundaries of the problem are explored and established, care is taken to avoid minimizing the relevance of the problem, as it is perceived by the client or by nurses. Eliciting involvement of clients and professionals at an early stage can reduce the risk of minimizing the problem, or even misconstruing what the problem is.

Literature Review

A thorough review of the literature is an essential part of the intervention development process. The results of this review determine the starting point of intervention development (see e.g. Ream & Richardson 1999). It clarifies the availability and quality of the building blocks. It also gives direction to an exploratory study that may need to be conducted before the initial version of the intervention can be written.

The review of the literature must be extensive. All levels of evidence concerning the intervention are reviewed. The following questions are central in the literature review:

- Is the nature of the problem clear, from both an objective and subjective point of view?
- Are the clients' needs and experiences concerning this problem area clear?
- Are there interventions for this or similar problem areas? Were scholarly methods used to develop existing interventions? Are there investigations

of the effects of the interventions? Are systematic literature reviews available?

- What is known about the implementation aspects of existing interventions? Can the intervention (or if necessary, a modified form of the intervention) be utilized in nursing practice? Is the intervention congruent with the competencies of nurses?
- Which interventions are acceptable to the client? What are the experiences of clients with the interventions?
- Is relevant theoretical knowledge available? Has previous research focused on theory or model development? Have existing theories or conceptual models been tested? Can existing theories or models direct future intervention development within the identified problem area?

The results of the literature review determine the subsequent course of intervention development, in other words, which additional building blocks are needed. The central question is, whether the available knowledge is sufficient to proceed to the Intervention Design stage and to begin to write a first draft of the intervention. Often it is not easy to determine this. Discussing the findings with colleagues and consulting experts may help the researcher to decide which strategies are necessary and how to proceed with the process of intervention development. An important criterion concerns the clients' perspective: is the existing knowledge of the client's perspective sufficient to develop an intervention that is acceptable to and valued by the client. Care must be taken to avoid concluding prematurely that there is adequate knowledge and insight available to commence with the Intervention Design stage. If there is limited or inadequate knowledge, then additional research, for example a Problem Analysis and or Needs Analysis, is indicated before designing the intervention can begin.

Problem Analysis

Sometimes nurses realize that there is a problem, however the nature of the problem is unclear. Because insight into the problem is fundamental to the process of intervention development, research efforts are warranted in order to understand the nature of the problem.

An example from a research project in progress follows:

Nurses are aware that partners of aphasic patients, who are also their care providers, are severely burdened. However, before developing an intervention to support these partners-caregivers, it is necessary to better understand the nature of their burden. General literature on caregiver burden or studies carried out with other populations is helpful. More essential to the researcher who develops the intervention is an understanding of the situation as experienced by partners-caregivers of aphasic patients. The better the researcher uncovers the processes that are at play in their experience, the greater the likelihood that a successful intervention can be designed (Kolk 2003).

Various research techniques can be applied in order to gain insight into the problem. Participant observation can be used to envision the manner in which the problem manifests itself in daily living and to understand the meaning of the problem for those who are affected. Also, observations can clarify how the affected individuals react to and attempt to solve the problem and which coping strategies are used to deal with the experienced problem. Individual or (focus) group interviews with nurses, clients and experts and qualitative analysis can be used in order to describe the experienced problems from the perspective of those involved. Additionally, in advance of the Intervention Design stage, the interviews with clients enable the researcher to identify possible methods of resolving the problem and to formulate the associated guidelines (see e.g. Joseph *et al*. 1996; Murdaugh & Sowell 1999; Gamel *et al.* 2001). Qualitative methods enable the researcher to initiate theory development. When inductive generalization techniques are used with the empirical findings from qualitative studies, concepts can be developed and explanations of observed relationships among the concepts can be examined. In this way, practical problems are placed within a theoretical context.

This descriptive (and eventually theory-building) research provides a definition of the problem and the various aspects that are associated with the problem. Furthermore it yields knowledge concerning the factors that cause and maintain the problem. This insight makes it possible to take the first step towards resolving the problem. When the problem analysis demonstrates that the problem cannot be resolved or can only be resolved partially, then the aim of intervention design will be promotion of coping with the problem (rather than resolving the problem). If the causes of the problem or the factors that maintain the problem remain unclear, then further research aimed at filling the lacunas must be done before proceeding with developing the intervention.

Apart from obtaining the most complete possible description of the problems that occur in the clinical situation, an image of the subjective experiences of the client is formed. These subjective experiences are of vital importance in the Intervention Design stage. Our proposition is, the better that an intervention matches the manner in which the problem is experienced by those involved, the more effective it is. This perspective necessitates an exploration of the problem as it is: 1) experienced by the client, 2) verbalized by the client (whether or not in the form of an explicit request for help) and 3) identified by the care-givers (nurses and other professionals). An analysis of the discrepancies among these three aspects provides important clues for the further development of the intervention.

Needs Analysis

Even when insight into the nature of the problem is available and a clear problem statement is formulated, there still may be inadequate information to ascertain what care is needed. The question, what type of care is desirable in order to influence the nature of this problem, may need further clarification.

Examination of research findings describing the clients' perspective of the problem is an intrinsic and essential part of the problem analysis. The expectation is, needs and requests for care flow naturally from the problems as perceived and experienced by clients. However sometimes the exploration of the problem does not result in clear statements of needs and explicit requests for help. In this case, the needs can be more precisely formulated through additional research. The effectiveness of a new intervention is directly determined by the degree to which the clients' needs and requests for care are taken into account during the intervention design stage. Several examples from needs analysis research from our department follow:

- *A well-known problem for patients with a depressive disorder is apathetic and inactive behaviour. Encouraging these patients to become active is a frequently used nursing intervention. Yet this intervention can have adverse effects in many cases. Feelings of depression may be reinforced or even intensified when patients with depression are unable to increase their activity level and consequently they feel inadequate. Retrospective research concerning the needs and requests for care of patients recovered from a depressive episode can reveal important information and insight into an*

effective manner of intervening with this type of inactive behaviour (research project in progress).

- *A basic assumption in parental participation is that parents must be stimulated to be present often and for prolonged periods so that they can take part in the "mothering care" provided to their child. However some parents of a chronically ill child prefer that nurses (temporarily) assume a number of these tasks. Misunderstandings and lack of understanding of one another's position may lead to a tense relationship between parents and nurses (Van Swieten-Duifjes 1998).*
- *Patients with cancer indicate that they want information about the effects of treatment on sexuality. Yet even when professionals encourage patients to ask questions, the patient may not know what to ask. In a qualitative study in which 13 women and 12 men participated, the situations were identified in which women with gynaecological cancer experience a lack of information and support. The study also revealed what type of information was necessary at what time period. Furthermore, differences in the patient's needs and those of her partner were identified (Zegwaard et al. 2000).*

Qualitative research is the most appropriate approach to study the diversity and complexity of clients' needs and requests for care. Just as in the case of research concerning the problem definition, the research is not just descriptive, there is also an explanatory component. The investigation clarifies the process of how needs and requests for care develop as well as it leads to plausible explanations for the process. In this manner, a contribution is made to theory development and testing concerning the intervention (see e.g. Dewettinck *et al*. 2001)

This type of research reveals the important client needs and requests for care that are specific for the identified problem area. The range and diversity, rather than only the dominant pattern, can be described and explained because qualitative methods are used. This insight is important for the subsequent stages of Intervention Design and Intervention Validation because those aspects of the intervention that can be utilized in most situations for the specific client group can be distinguished from those aspects that need to be individualized. Furthermore, when theory-building research is also conducted in the stage preceding Intervention Design, then it is possible to give a rationale for the generally used versus individualized actions.

Current Practice Analysis

Often in their daily practice, nurses develop strategies to solve the encountered problems and identified needs of clients. Their answers are based primarily on 'common sense', practice experience and analytical reasoning.

Identification of existing intervention practices is valuable during the process of developing evidence-based interventions. These practices can be further developed and refined using scientific methods. Analysis of existing intervention practices is also useful because lessons can be learned from the accumulated experience.

The primary goals of studying intervention practices are: to identify the different types of interventions that nurses are using, to describe how the different types of interventions are used in practice and to gain insight into the experiences of providers and clients with available interventions. An example follows:

The experiences in practice were examined during the development of a nursing intervention aimed at early recognition of a psychotic relapse in clients with schizophrenia. A field exploration led to an inventory of sites in The Netherlands where early recognition interventions had been developed and were used in mental health care. Research with patients, family members and professionals was conducted to explore the existing practices and experiences. It was especially important to create a clear picture of the facilitating and restrictive factors that influence effective use of the intervention. This knowledge was invaluable in the further development and refinement of the intervention (Van Meijel et al. 2002b/c)

Several methods can be used for Current Practice Analysis. Researchers have used interviews with (expert) nurses and clients, the critical incident method and participant observation in order to describe existing practices (see e.g. Jenny & Logan 1991; Narayanasamy & Owens 2001; O'Connor 2000; Struthers 1999). When existing practices are studied, merit is given to the practice and experiential knowledge of nurses and other health care professionals. Not using this knowledge is a missed chance. Insight into existing practices offers a concrete point of departure for outlining the specific aspects and actions associated with the intervention. When care is taken to maximize the variation among participants, as far as personal characteristics and the contextual variables are concerned, it is possible to identify specific

aspects and actions associated with the intervention in diverse situations. This allows for optimal individualization of the intervention.

Intervention Design

As described in the previous section, the raw material or the building blocks needed to develop a nursing intervention are derived from the review of the literature, and where indicated, additional qualitative research. The goal of the Intervention Design stage is to formulate a first draft of the intervention.

The most general question is, which theoretical or conceptual frameworks are available to direct further intervention development. The literature review provides an answer to this question. When available, theoretical or conceptual frameworks are used in the design stage to operationalise the intervention, or in other words, to specify the associated actions: what should be done when, where, how and by whom.
Two illustrations follow:

When designing a nursing intervention for preparing patients for a threatening procedure (gastroscopy), Van Vliet (2001) applied two frameworks, The Theory of Self-Regulation (Leventhal & Johnson) and The Monitoring Process Model (Miller et al). This resulted in an intervention that was further specified for two patient subgroups. The so-called 'blunters' received only essential information because they prefer to minimalize the anxiety associated with excessive information. In contrast, the 'monitors' were given extensive information because they seek information about the procedure in order to reduce the anxiety associated with the unknown.

The Vulnerability-Stress Model is a generally accepted framework used in researching and treating schizophrenia. This was used by Van Meijel et al. (2000) to design an intervention directed at early recognition of psychotic relapse in patients with schizophrenia.

Existing theories or practice models, however do not always match the goal of the intervention under development and sometimes they have not been tested. In this case, relevant concepts can still be used to form recommendations for nursing actions because the recommendations and

associated actions are tested in the subsequent stage of intervention development. An example:

When developing a sexual teaching intervention in order to prevent sexual problems, a number of theories and practice models were identified during the literature review. For example, anticipatory guidance theories are relevant when preparing patients for not yet encountered situations, but sexual teaching must also encompass already encountered situations. Also health care professionals frequently use the PLISSIT Model to help them respond to sexual problems identified by patients. However the PLISSIT Model has not been investigated. Furthermore the underlying assumption that a nurse intervenes after a patient reports a sexual problem is not completely consistent with the intervention under development, namely a nurse initiates contact in order to provide information before sexual problem(s) develop. In this situation, 15 recommendations were formulated from the literature review and these recommendations and the associated actions were investigated in a field study in order to identify which concepts explain the value of the intervention (Gamel 2000).

In addition to using theory and conceptual models, designing the intervention is also facilitated when basic assumptions are formulated. They direct the use of the intervention in practice. Basic assumptions are general in nature and are applicable to the entire intervention. Basic assumptions can be formulated concerning topics such as the philosophy of care, the attitude towards the client and the role of informal caregivers within the intervention.

The next step is to determine if the intervention is in fact a compilation of separate interventions. In our work with intervention development, we have found that complex interventions (almost) always consist of a clustering of separate interventions. Especially with complex interventions, it is important to specify when multiple interventions need to be used in order to obtain the projected results and outcomes. Based on a review of research and clinical practice reports, Gamel (2000) designed a sexual teaching intervention that consisted of three clusters of multiple interventions. The first cluster specified interventions associated with the content (which information needs to be provided), the second focused on how to provide the information (which communication techniques to use) and the third cluster identified organizational aspects (how to prepare for a sexual teaching session).

Once the (clusters of) separate interventions are identified, then the associated concrete nursing activities are described. A theoretical rationale for the actions is given when sufficient evidence was found in the previous literature review or previous research. A rationale is essential because it provides insight into how the projected results or outcomes can be achieved with this intervention. Furthermore, it allows for a justified modification of the intervention when necessary. During the design stage, adequate attention is given to the feasibility of using the intervention in nursing practice. A compromise is sought between the detailed nuances that are suggested within the literature and the depth and complexity, and ultimate negative influence on feasibility, associated with such nuances.

A possible final step within the design stage is a review of the drafted intervention by experts, for example those who will receive the intervention (clients) or those who will use it (nurses) (see e.g. Rakel 1992). Experts, based on their experience and knowledge, can provide valuable feedback about the content of the intervention and the feasibility of using it. Using their feedback, the last modifications in the proposed intervention can be made and then it is ready for testing in practice.

Intervention Validation

While developing the rough draft, the available evidence is evaluated in order to mould the content and form of the intervention in accordance with the current state of knowledge. The newly designed intervention can now be tested in clinical practice (see e.g. Morse *et al*. 2000; Walker *et al.* 1989; Gamel *et al*. 2001).

A proven method of first testing of an intervention is a qualitative evaluation using case studies. The first step is to select cases in which the intervention can be used. When choosing cases, the researcher maximizes variation in client and context variables. The goal of the qualitative evaluation is to test the intervention in diverse situations, which are characteristic of those with which the nurse is confronted in daily practice. Once the cases are selected, the intervention is used and interviews are conducted in order to obtain data about the experience with the intervention. As previously described, often an intervention is complex and it contains clusters of multiple interventions. If so, it is imperative to evaluate each separate intervention and

the associated actions as well as the entire combination. In this way, data are collected that are used to make concrete modifications in a part of the intervention as well as in the intervention in its totality.

Furthermore, the insight in the contribution of the separate interventions is essential before an RCT is conducted because in an RCT the effect of the intervention in its totality is investigated. If an RCT demonstrates that the intervention is not effective, it is unclear if the entire clustering of interventions is not effective or if only one intervention or some of the associated actions are ineffective. Moreover even when the intervention is shown to be effective, it is not clear if and to what degree the separate interventions contribute to the effect.

The qualitative evaluation aims to answer the following three central questions:

- How does the client experience the intervention (including all parts or actions)?
- While carrying out the intervention or afterwards, which effects are observed by nurses or experienced by clients?
- How do nurses judge the feasibility of the intervention?

As answers are sought to these questions, an attempt is made to identify the explanatory factors. Identifying determining factors and plausible explanations help to create understanding of the conditions that are necessary in order to achieve the results and goals projected for the intervention.

Usually, qualitative evaluation leads to modifications in the parts and separate actions associated with a complex intervention. If so, new cases are sought for re-testing and further evaluation. This procedure is carried out until the form and the content of the intervention are optimal.

Randomised Controlled Trial

After the Intervention Validation stage, empirical data supporting the intervention already exist because of the rigorous procedures that were followed during the development process.
The building blocks of the intervention were carefully selected and they were tested for value and usability. The intervention can be further tested in a RCT.

Before doing so, the question needs to be answered, whether it is expected that the additional evidence accrued with a RCT will justify the costs (time and personnel) that will be incurred. There is no universal answer to this question. A useful strategy to answer the question is to determine whether or not the following conditions have been met:

- the intervention has been developed in a scientifically sound manner,
- the value of the intervention for the clients has been demonstrated,
- the targeted results were apparent in a qualitative evaluation,
- the intervention is feasible in practice and
- other health care professionals, based on their practice knowledge, are convinced that the intervention is needed.

When these conditions have been met, we assert that the researcher should probably focus on other more urgent health care problems than a RCT of the newly developed intervention. The a priori probabilities that it will be successful are indeed high.

If additional (scientific) merits of a RCT are identified, another question - an ethical one - still needs to be answered. Can the newly developed intervention, about which some evidence of its value and feasibility already exists, be withheld from participants in the control group? This is also a question for which there is no simple answer. The researcher and ultimately a medical ethical committee must deliberate over the merits of a RCT. Do the potential gains outweigh the possible disadvantages of not providing the intervention to the control group? When the degree of certainty concerning the effectiveness of the intervention is insufficient to warrant implementation in practice, the researcher will likely decide to conduct a RCT.

Most times, numerous methodological problems must be solved if a (quasi-) experimental research design is used. These are inherent to the so-called pragmatic trials in which the effectiveness of an intervention is investigated in a naturalistic setting (Algra &De Graaf 1999). For example, the most relevant outcome variables and available measures to test for their presence must be selected. Another problem is the selection of research participants and the often limited possibilities for pure randomisation within a field experiment. Also the influence of confounding variables may be difficult to identify and it is challenging to maintain control over these variables, especially when the RCT is carried out at multiple locations. It also may be a tremendous task to ensure that the nursing intervention is adequately and

sufficiently implemented in practice for a long enough period to achieve a satisfactory statistical power. These issues, in combination with the limited control of the researcher over the actual use of the intervention in practice and the contamination between experimental and control groups, illustrate that the problems associated with carrying out an experiment are extensive. Careful consideration is indicated when making methodological choices in order to increase the interpretability of results gained from the RCT.

An example is presented of a situation in which a RCT is indicated:

In a research study concerning the development of an intervention aimed at early recognition of psychoses in patients with schizophrenia, after a review of the literature an investigation of current practices was conducted. Based on these findings, a first draft of the intervention was written. Experts from various disciplines evaluated the intervention protocol. Then the intervention was investigated for feasibility of use in practice and effect in nine case studies. Finally a RCT was carried out with 92 participants equally distributed over the experimental and control group. The primary outcome measures are the presence of psychotic relapse and (hospital) admission.
The most important reason to undertake a RCT in the presence of the accumulated evidence was that the effectiveness of the intervention, the reduction of psychotic relapse, can not be judged but by comparison. The availability of clear outcomes as well as the methods and instruments to measure these variables made a RCT feasible. Quantification of the effects using a RCT is needed in order to make these effects clearly visible.

In conclusion

In this article, one model for developing and testing nursing interventions is presented. The model is appropriate for complex interventions in which the experience of the client plays a vital role.
The way in which qualitative research contributes to the intervention development process is explicitly described. A theory-based intervention can be developed because attention is given to theory development and verification in the various stages of intervention development. The importance of RCTs for testing effectiveness of complex nursing interventions is not negated, however critical questions concerning the justifiability of a RCT are raised. The arguments and illustrations in support of qualitative research presented in this article can be used to oppose the position of some critics that

the popularity of qualitative research within nursing is a reflection of a fashionable trend or the early developmental stage of nursing science. Qualitative research makes an essential and lasting contribution to the development of knowledge and testing of theory within nursing.

Chapter 4

The practice of early recognition and early intervention to prevent psychotic relapse in patients with schizophrenia: An exploratory study (Part 1)

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Abstract

In this article we describe the findings of an exploratory study into the application of early recognition and early intervention methods aimed at the prevention of psychotic relapses in patients with schizophrenia. We address several models of relapse prevention plans and indicate how patients, health care professionals and other persons involved may be able to list and evaluate early warning signs systematically. We also pay attention to the role of the patient's family and to the potential effects of using early recognition and early intervention methods. In chapter 5 (part 2), we will focus more specifically on factors, which favourably or adversely affect the use of early recognition and early intervention methods.

The results of this exploratory study will be used to design an intervention protocol for nurses to prepare relapse prevention plans with the individual patients and his social network.

Introduction

Preventing psychotic relapse is an essential element in the treatment program for patients with schizophrenia (APA 2000). The psychotic episodes place a heavy burden on the patients and their environment. A psychosis adversely affects a patient's psychosocial functioning. Furthermore, psychotic relapse (and the professional treatment and counselling it requires) involves significant financial costs (Evers *et al.,* 1995; Novacek & Raskin, 1998; Buchanan & Carpenter, 2000). Although adequate antipsychotic medication is vital, psychosocial interventions are also necessary to reduce the risk of relapse. Possible options are psycho-education, family support and skills training.

In the first year following discharge, about 70% of the patients who do not receive any treatment will suffer a relapse (Kissling 1991; Kissling 1992; Ayuso-Gutierrez *et al.* 1997; Kane, in APA 2000). This figure drops to approximately 40% if patients receive regular treatment, that is antipsychotic medication combined with basic psychosocial counselling (Kissling 1992; Liberman & Kopelowicz 1995; Viguera *et al*. 1997), although it may be up to 60% in families with a high level of expressed emotion (Tarrier 1997). Medication non-compliance is a major risk factor in the occurrence of psychotic relapses (Downs George *et al.* 1996; Fenton *et al.* 1997; Marder 1998; Dobber *et al.* 2001). In case of optimal drug treatment and compliance, in combination with adequate psychosocial interventions, the relapse rate can even be reduced to 20% (Kissling 1991, 1992; De Haan *et al.* 1997). In other words, in current psychiatric practice there still remain opportunities to reduce relapse rates by further development and optimal utilization of biological and psychosocial interventions.

With regard to relapse prevention in patients with schizophrenia, in the past few years early recognition and early intervention have become subjects of growing interest. The focus is on a preventive strategy of rapid intervention if there are early warning signs of the onset of a psychosis (prodromal symptoms). The aim of early intervention is to restore the balance in a patient. Such interventions may consist of alterations of the medication regimen or may be psychosocial in nature (Herz *et al.* 1989; Herz 1990; O'Connor 1991; Birchwood *et al.* 1992; Wiedemann *et al.* 1994; Van Meijel 1996). The warning signs and the necessary interventions can be written down in a relapse prevention plan to be shared with all those who are involved in the patient's

treatment and care: the patient himself or herself, health care professionals, family members and friends.

Prodromal symptoms are highly diverse and vary greatly from person to person (Herz & Melville 1980). They may be very general in nature (such as anxiety, agitation, dysphoria, mistrust), but may also consist of very specific behavioural patterns that manifest themselves in the preliminary phase of a psychosis (wearing eccentric clothes or flamboyant hairstyles, for instance). Behavioural patterns of this kind are also referred to as idiosyncratic behaviours (Herz 1990; Hamera *et al.* 1992; Herz & Lamberti 1995; Norman & Malla 1995; Campo & Merkelbach 1996).

The relevance of these warning signs to clinical practice is still discussed. There are several publications, which question the predictive value of early warning signs (Marder *et al.* 1986; Gaebel *et al.* 1993; Norma and Malla, 1995). The main point of dispute concerns the degree of probability that a psychosis will actually occur if any of the prodromal symptoms are observed. The chance of a psychosis being preceded by early warning signs is another issue that is discussed. Because of the different research methods and the different operationalisations of concepts like "early signs" and "relapse", the answers to these questions have thus far proved to be rather inconsistent.

Several articles on early recognition and early intervention have been published in the past few years (for a summary, see O'Connor 1991; Bustillo *et al.* 1995; Herz & Lamberti 1995; Norma & Malla 1995; Van Meijel 1996). A limited number of studies have been conducted into the effects of different medication strategies (continuous versus targeted medication), combined with early recognition and early intervention (Herz et al. 1982; Carpenter & Heinrichs 1983; Heinrichs & Carpenter 1985; Hirsch & Jolley 1989; Hirsch et al. 1989; Jolley et al. 1989; 1990). As the early recognition techniques used in these studies were either very basic or were described only very summarily, these studies do not offer much insight in these methods.

Studies conducted by Liberman's research group (for a summary, see Arends *et al.* 2000) and by Herz *et al.* (2000) into the effects of relapse prevention programmes show that there is ground for some optimism in terms of psycho-educational effects, readmission rates and relapse rates. The American Psychiatric Association (APA 2000) has expressed the opinion that early recognition and early intervention to prevent psychotic relapses should form part of all treatment programmes.

Given the often prolonged care provided to schizophrenic patients by nursing staff, nurses are in a position to play a crucial role in early recognition and early intervention (Van Meijel 1996). At this point, however, too little is known of early intervention methods that can be successfully applied by nurses. The first step to be taken, therefore, is to learn what early intervention methods are available and which factors may influence their effective use. This article describes an exploratory study that was conducted to gain a better understanding of the issue. The research questions are:

- How are relapse prevention plans used in current psychiatric practice?
- How do health care professionals, patients and family members experience the use of relapse prevention plans?

In this chapter (part 1) we describe several models of relapse prevention plans, the way early warning signs can be systematically listed and ways of monitoring these early signs. Subsequently, we discuss the role of the family with regard to working with relapse prevention plans. Finally, we examine the potential effects of using early recognition and early intervention methods. In chapter 5 (part 2) we discuss a number of factors that influence the effective use of these methods.

The results of this exploratory study will be used for developing and testing a nursing intervention protocol for early recognition and early intervention; to be used in individualized nursing care for patients with schizophrenia.

Methods

The study used 25 interviews with health care professionals, patients and their families from six different treatment settings in the Netherlands. The settings were selected by consulting two sources. The first source consisted of experts who were asked whether they knew any treatment settings in which early intervention methods were systematically used with schizophrenic patients. The second source was an exploratory field study conducted by Van Mierlo (1997) to map current activities in the field of "symptom management in schizophrenia" in the Netherlands. Given the purpose of the present study, it was very important to select a number of settings with a certain degree of variance in the nature of the setting, the methods used for early intervention

and the characteristics of the target group. This would ensure that a wide range of experiences was included. Six treatment settings were chosen: (1) an outpatient clinic of a psychiatric hospital, (2) a unit for chronic patients at a psychiatric hospital, (3) a unit for outpatients at a university hospital, (4) an adolescent outpatients clinic at a university hospital, (5) an outpatient clinic attended by clients of a RIAGG (regional institute for community mental health care) and (6) a case management project of a RIAGG.

Health care professionals were invited to take part in semi-structured interviews making use of topics based on a literature study. A total of nine interviews were held (five psychiatric nurses, one psychiatrist, one psychologist and two general physicians). The interviews lasted from one to two hours. Written documentation was collected to supplement the interviews.

Following these interviews, the patient databases of four treatment settings were used to select patients who had experience with the early intervention methods used. Two settings were excluded from the study because they had not used early intervention methods long enough for the patients to have any real experience with them. The criteria for inclusion of a patient were a positive diagnosis of schizophrenia, the absence of manifest psychotic symptoms and an ability to express his or her experiences verbally. The target group consisted of patients who benefited from the early intervention strategy in varying degrees, so as to obtain a broad range of different experiences. In consultation with the health care professionals, eight patients (seven men, one woman) were selected in this way. Their average age was 30 (range: 21 - 39). Their case history covered a period of 6.5 years on average (range: 2 - 17 years). The number of psychotic relapses varied from one to five. There were three patients whose relapses could not be established clearly because they had persistent positive symptoms. Open interviews lasting 45 to 60 minutes were held with the patients. The relapse prevention plans (if available) formed the basis for the interviews. The patients were asked questions about the content of their plans, how the plans had been drawn up and whether they benefited from their plans. If patients did not have a plan, the focus was on aspects such as the impediments to preparing a plan and the possible added value such a plan could have for them.

The patients were asked whether they had any objections to their families being approached for an interview. All patients gave permission. Eight interviews were held with fifteen family members (fourteen parents, one

sister). In an open interview they were asked questions about their involvement and experiences with early recognition and intervention.

The interviews were recorded on audiotape, and written verbatim transcripts were made for analytical purposes. Data collection and data analysis were carried out in a cyclical process in which the data analysis guided the data collection of subsequent interviews. The analysis was made using WINMAX-PRO '96 (Kuckartz 1996).
The analysis was made by:

1. Interpretation of each separate text (single case analysis);
2. Interpretative comparison of single cases (comparative single case analysis);
3. Development of a system of thematic categories (with the aid of code words);
4. Allocation of codes to text segments;
5. Compilation and interpretation of segments with the same codes (thematic analysis);
6. Analysis of the relationships between the codes and themes (comparative thematic analysis).

By using these research methods insight was gained in the processes of application of early recognition and early intervention strategies in mental health care. The purpose was to obtain data that could be used for further protocol development. The sample size was adequate to achieve this goal. By interviewing experts in the field of early recognition and intervention who had prolonged experience in using this intervention strategy, the most crucial information to be used in future protocol development was efficiently obtained. The data received from interviews with patients and family members partly confirmed the statements of the mental health carers; on some items new information was obtained from their specific perspective. During the last interviews no new crucial information could be added to the categories and themes described during former data analysis, so we concluded that saturation was reached to a sufficient extent.

Results

Relapse prevention plans

The relapse prevention plans, used by mental health workers, show great variation in terms of both form and content. If we break the plans down into their component parts, they can be classified into three models, although hybrid models are used in certain settings.

1. The basic model: This model confines itself to listing the early warning signs as accurately as possible. The lists are compiled either in an open interview with the patient or using a checklist of common signs. In most cases, the early signs that are relevant for a specific patient are written down in the patient's record or on a specially designed card, which the patient may carry with him. The card may also state the name of the health care professional to be contacted by the patient if any of the early signs occur. This model thus collects the most elementary information required for early recognition and early intervention purposes. Intervention usually consists of adjustments of antipsychotic medication. The patient's role is relatively passive, while a medical and psychiatric orientation is dominant.
2. The phase model: This model is designed to provide a detailed reconstruction of the various phases of previous psychotic episodes in order to create an overall picture of a psychotic episode, from the moment of (relative) stability until the onset of a florid psychosis. This model operates on the assumption that subsequent psychotic episodes will show a similar pattern. Interventions are linked to each phase, and aim at keeping a patient in balance or at restoring the balance. The key question is always whether the patient can act independently or whether he or she needs professional help. This model aims at using as fully as possible the patient's own coping skills. Compared to the basic model, it requires a more active role of the patient.
3. The comprehensive model: This model not only focuses on prodromes and symptoms, but also systematically records factors that have a direct or indirect impact on the onset of psychotic relapse. Stress factors are identified in terms of internal sources (e.g. unrealistic targets) or external sources (e.g. stressful interactions within the family). Protective factors are also charted, making a distinction between protective social factors (e.g. supportive contacts with friends) and protective activities (e.g.

recreational activities or sports). Other elements are the patient's skills (e.g. degree of assertiveness) or lack of skills (e.g. personal hygiene), which can be improved with training. The presence or absence of these skills can have an impact on the stress levels experienced. Finally, the model identifies the nature of any disturbing or undesired behaviour that may unsettle the patient. The patients (and their social environment) are thus able to gain insight into a great number of influencing factors. This enables them to decide which measures to take, in both preventive and curative terms, in the event of a psychotic episode. The comprehensive model is dynamic in nature and less prescriptive than the other two models, as it does not set forth in detail what to do when specific prodromes occur.

The most striking difference between the three models is the demands they make of the health care professionals and of the patients and their families. For instance, the first model confines the identification of prodromes to a mere listing of warning signs, while the second involves a more complex activity, reconstructing a process and defining certain phases in it. The actions or interventions also differ: the first model focuses exclusively on contacting the treating psychiatrist, who will then intervene by adjusting the medication, whereas the other models demand that the patient plays a more active role: The patient has (more or less) insight into his own situation and from that he is capable to adjust his behaviour and ask - if necessary - for professional help. The emphasis is on a combination of pharmacological and psychosocial interventions.

Listing of Early Warning Signs

To assess the content of the relapse prevention plan, the patients were asked about the major signs, which heralded the onset of a psychosis in their specific situations. The answers given in the interviews were compared with the contents of the relapse prevention plans. Family members were also interviewed about relevant major warning signs.

Most of the patients and their family members were well able to describe the changes that occurred in the period preceding a psychosis. On the other hand, the degree of conformity between the lists made by patients and those of their family members did vary. In a number of cases, the patients and their families were almost in full agreement about the major warning signs,

particularly if the family saw a clear role for themselves in early recognition and intervention. In those cases, the family members made efforts to obtain the requisite knowledge, and the mental health worker, the patient and his family worked together to achieve a certain degree of consensus on the most important warning signs.

The patients themselves were very well able to define the prodromes that directly referred to specific complaints (e.g. sleeping disturbances) or to feelings of anxiety or dysphoria, but they were less able to identify pre-psychotic symptoms (suspiciousness, delusions, changing perceptions). Families were better equipped to observe such pre-psychotic symptoms because they frequently involved a change in the patient's behaviour. Some of the families attributed the patient's reduced ability to recognise his own pre-psychotic prodromes to a diminishing insight as the process of psychotic decompensation progressed.

In addition to the pre-psychotic prodromes, there were other issues on which disagreement occurred. Parents often observed that their child was less concerned with personal hygiene or housekeeping when he or she went through a prodromal phase; patients never mentioned this. Furthermore, family members relatively often pointed out the patient's uninhibited and euphoric behaviour during this phase; the patients failed to mention this. It seems likely that self-perception is limited in these respects during the prodromal phase, although the possibility should not be ruled out that patients do not consider these prodromes to be inconvenient. On the contrary, the prodromes may be experienced as pleasant, so that patients see no reason to make a problem of the signs.

There were a few cases in which the parents proved to have limited insight into the inner world of their child during a pre-psychotic phase. A patient's sense of unreality, difficulty with structuring thoughts, fears of insanity, gloominess: these are just a few examples of the changes that take place in a patient's subjective perception, that are often not shared with people in their environment and that are more often than not impossible to deduce directly from the patient's observable behaviour. Because they withdraw more and more into their inner world – both physically and emotionally - in the pre-psychotic phase, patients hide these prodromes even better. In the phase in which warning signs are listed, the information offered by people from the patient's environment frequently complements the information provided by the patient, and vice versa.

Our study showed that a number of patients suffered from psychotic symptoms for a prolonged period of time. To them, the distinction between prodromal and psychotic symptoms is of less importance. The phased development of psychosis is not very recognisable to these patients. Their disturbed frame of mind during pre-psychotic and psychotic experiences also affect their ability to structure their own reality, thus complicating even further the reconstruction of the prodromal phase - if it is recognisable at all.

The significance of idiosyncratic behaviour for early recognition was confirmed by the practice of listing early signs. Some of the patients and their families explicitly referred to this type of warning sign and attached great predictive value to them. Examples include a patient who, in the prodromal phase, suddenly started to use his bicycle instead of driving his car, or a patient who started to smoke more than usual; there was a patient who felt the urge to write a book on arithmetic, and another patient who in the prodromal phase turned up his hifi system and thus caused a great deal of nuisance.

The interviews showed that, when existing scales or lists of early warning signs were used as a tool for the patient, it entailed the risk of losing sight of the distinction between truly important signs and secondary signs: a great many signs from the scale were recognised and declared applicable. When these scales were used, the signs were formulated in the language of health care professionals, rather than in the patient's own language. In one setting, experiments with the lists gradually led to them being used less and less. They came to be used more as a checklist to verify that all crucial signs had been taken into account.

Monitoring

Monitoring is the more or less systematic assessment of the presence of early signs for the purpose of estimating the risk of a psychotic relapse. We asked patients to describe how they performed this monitoring. It appeared that a distinction could be made between two types of monitoring:

(1) Direct monitoring, in which the presence or absence of early signs is assessed directly. The patients give scores to the listed prodromes, for instance on a five-point scale (monitoring by scoring). In some instances, patients show such insight into their early warning signs that they have every confidence that an alarm will go off if any of them occur. These patients consider a paper

scoring method redundant. We might call their method one of permanent self-observation.

(2) Indirect monitoring, in which actual situations are assessed to monitor the presence or absence of protective or stress factors. For instance, one of the patients believed that his medication together with the regularity of life provided by steady work offered sufficient protection against psychotic episodes. If these circumstances were to change, he would consider it a reason to start direct monitoring. Another example was a patient for whom falling in love had been a significant stress factor in the past. If he were to fall in love again, he would also consider switching to the direct monitoring method.

With the exception of one patient, all interviewees were optimistic about their own ability to prevent psychosis in the future. The parents were not so convinced - given their earlier experiences - that their child would be able to observe the signs properly. They believed that their children overestimated their own capacity of early recognition. Indeed, in their experience, at the crucial moment the patients were unable to recognise the prodromes, they failed to interpret the prodromes correctly or could not take the appropriate measures.

The conclusion to be drawn is that indirect monitoring might be effective, but primarily if it is combined with a form of direct monitoring. It is well known that psychotic episodes may occur despite protective factors and that they may occur even if no specific sources of stress can be identified in the pre-psychotic phase. Furthermore, permanent self-monitoring may well be effective only if the patient has first kept score of the warning signs for a longer period of time. Monitoring by scoring makes it easier to recognise early signs at crucial moments. Another factor to be taken into account is that some of the patients are unable to identify early warning signs in the phase leading up to the psychosis or are unable to interpret the signs properly. This group will have to rely increasingly on others to detect the signs and to intervene early. The role of the family in early detection and early intervention will be discussed in the section below.

Role of the Family

In most settings, informative meetings are organised in which attention is paid - to varying degrees - to the issues of early recognition and early

intervention to prevent psychotic relapse. Such meetings promote the involvement of families in the subject. However, if we look at the way in which the general information is translated into relapse prevention plans for the individual patients, it is apparent that families are not systematically involved. All of the health care professionals interviewed regarded the family's involvement as very important because (1) families can supply significant additional information on prodromes for the relapse prevention plan, (2) families can help monitor the condition of patients, especially when a patient's perception of his disorder deteriorates, (3) parents can describe their own experiences with their children in times of threatening or actual psychotic crises, and these experiences can be helpful in preparing and executing an action plan, and (4) it often depends on the response of the families whether or not adequate help is enlisted. There are a great many situations, however, in which the crucial role of the family is not translated into concrete practical actions on the part of the health care professionals.

The interviews with patients and their family members revealed that family members were actively involved in the care for the schizophrenic patient. Therefore, in many cases co-ordination of the activities undertaken by health care workers and family members seems more appropriate than to encourage family members to take more action. Parents had quite frequent contacts with their sons or daughters, varying from once a week to once a day, often supplemented by a number of telephone calls per week. This allowed them to monitor their child's condition very closely. They were strongly committed and very concerned. Eleven of the fifteen parents indicated that they worried about their children's condition "quite a lot" to "very much". Their main concerns were the fear of new psychotic episodes, the fear of suicide, the fear of their children getting into trouble in their everyday life and the future prospects for their children.

Some of the parents were convinced that they were able to detect an impending psychosis early, but there were other parents who indicated that they had trouble identifying relevant signs as opposed to natural variations in their son's or daughter's behaviour. Their perception of the situation, however, is decisive for the response to it. A hasty reaction may lead to unnecessary agitation and patronising, a late response will prevent the necessary help being given.

Despite the fact that patients considered themselves well equipped to detect prodromes early, most of them attached much value to their parents' availability. They often expressed contradictory opinions in this respect. In a broad sense, they claimed that they were well capable of early recognition and early intervention, but their actual stories frequently showed that they had to rely on their parents here. Most parents regarded their availability as self-evident, while often also qualifying it as a burden. The ever-recurring need to be at the "beck and call" of their son or daughter and the lack of reciprocity within the relationship were termed burdensome by all of them. The quality of the relationship between parents and child appeared to be a significant factor influencing the level of pressure experienced and hence the willingness to help.

The conclusion is that parents have a great deal to offer in the fields of early recognition and early intervention, that they actually take a great deal of action in practice, but that the co-ordination between their activities and those of the health care professionals still needs structuring.

Effects of early recognition and intervention

Health care professionals, patients and families listed a whole range of effects, which they claimed were triggered by early recognition and early intervention. Most of them referred to an increase in the patient's self-management. Patients were able to manage their illness better and were thus able to prevent or delay a psychotic relapse and a potential readmission to hospital. Patients were much less at the mercy of all kinds of inexplicable and unmanageable symptoms, which increased their feelings of autonomy and reduced their dependence on others. A number of patients indicated that their self-confidence had improved because of their higher level of self-management. The patients also learned that psychiatry was more than "just pills" and that there were many psychosocial opportunities to cope with the disorder and its consequences. Health care professionals, however, put the issue of self-management in perspective. Little is known about the effects of early intervention on the course of schizophrenia and it would be improper to hold the patients overly responsible for the way their disorder develops. Feelings of guilt in patients if they have a new psychotic episode - despite all efforts aimed at early recognition and intervention - should be avoided.

Both patients and health care professionals indicated that patients did learn better to define the nature of their experiences during the pre-psychotic phase. Patients realised what was happening to them and were thus able to make appropriate choices to respond to changing subjective experiences. Feelings of competence result in a lower level of anxiety. Anxiety can be a stress factor that worsens existing prodromes or symptoms, leading to a vicious circle of growing stress and increased symptoms.

Understanding these prodromal experiences leads to less feelings of guilt in a patient and prevents self-accusation, as he will be able to identify the disorder as a cause for a deterioration of his condition and will not - as he was wont to do - attribute it to his own personal failure. One of the patients described how he learned to cope with the feelings of suspicion, which always heralded the onset of a psychotic episode. Instead of being carried away by the alleged hostility of his surroundings, he was able to be more objective. He now calls upon others to help him instead of turning against them.

One of the major reasons for the growing sense of self-management is the fact that patients are offered a framework in which they are better able to understand the causes and effects of their own behaviour. The comprehensive model in particular focuses on this aspect. Patients are taught how to link stress factors, their own conduct and early symptoms. It is expected that this will have an educational effect on the patients and other persons involved.

There were several health care professionals who observed that patients felt more relaxed if they could rely on agreements made in the relapse prevention plan and did not have to face any changes for the worse on their own. Patients also felt more relaxed if they were able to objectify their own situation by means of early warning signs. They felt at ease in the absence of early signs.

In situations in which early recognition and early intervention were applied successfully and relative stability was achieved in a patient, the focus could be shifted to long-term goals in terms of the patient's living and working environment or recreational activities. If a patient suffers consistently from psychotic relapses, his day-to-day routine will be interrupted time and again and it will often be difficult for him to resume his own life.

A number of patients experienced the relapse prevention plan as a tool to communicate with others, to talk about what was wrong with them, what kind of help was needed and how that help could be offered in specific situations. Particularly for patients with cognitive limitations who have trouble collecting their thoughts, the relapse prevention plan could serve as a

"prosthetic cognitive schedule." One of the health care professionals reported that patients were more open and communicative if the interaction between the health care professional and the patient was defined by a clear goal, which the patient regarded as useful. This was completely contrary to the unstructured and random conversations that sometimes took place between professionals and patients in the context of the current care programme and that might affect a patient's motivation to undergo treatment.

Significantly, none of the three groups of interviewees saw a link with their medication, in the sense that proper monitoring and relative stability might constitute a reason for reducing their medication.

Relapse prevention plans not only have an effect on patients, but also on their parents. The actions included in the plan serve as a guideline for parents to deal with their child in the event of an impending or actual crisis. Parents find it safer to distance themselves from their child if they are convinced that proper agreements are in place about who will take action in case of a pending crisis. In this way, the relapse prevention plan operates as a tool to delegate care. The parents of one of the patients, for instance, stated that they finally felt they could go away on holiday now that they knew that suitable arrangements would be included in the relapse prevention plan.

Health care professionals also referred to a number of additional effects of working with relapse prevention plans: awareness among patients of each other's relapse prevention plans could have a positive effect on their interaction. They could monitor each other's signs, which was particularly important in situations where nursing staff was available only to a limited extent (in sheltered living environments, for instance). The plans enhanced their understanding of each other's behaviour and helped avoid the escalation of group interactions.

As for the relationship between health care professionals and patients, the plans defined the mutual responsibilities more clearly; describing what is to be expected both of the patient and of the health care professional in an imminent crisis. This brings about a situation marked by co-operation and dialogue rather than the classical situation of "… the health care professional asking questions and the patient answering them."

Finally, for the health care professionals themselves, the relapse prevention plans ensured a uniform and clear approach towards the patients because of the agreements recorded in the plans.

Conclusion

In this article (part 1), we described the findings of an exploratory study into the application of early recognition and early intervention methods for schizophrenic patients in the Netherlands. We addressed several models of relapse prevention plans and indicated how patients, health care professionals and other persons involved may be able to list and evaluate early warning signs systematically. We also paid attention to the role of the patient's family and to the potential effects of using early recognition and early intervention methods. In chapter 5, we will focus more specifically on factors, which favourably or adversely affect the use of early recognition and early intervention methods. The results of this exploratory study will be used to design an intervention protocol for nursing staff to serve as a tool for preparing symptoms recognition plans with the individual patients and their social networks.

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Chapter 5

The practice of early recognition and early intervention to prevent relapse in patients with schizophrenia: An exploratory study (Part 2)

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Abstract

In this article we describe the findings of an exploratory study into the application of early recognition and early intervention methods aimed at prevention of psychotic relapses in patients with schizophrenia. Following the results we described in part 1, we now focus specifically on factors, which favourably or adversely affect the use of early recognition and early intervention methods. The following issues will be addressed: (1) information and education, (2) attitude of health care professionals, (3) the patient's insight, (4) acceptance of illness, (5) motivation, (6) other relevant patient characteristics, and (7) continuity of care. Finally, the implications of the findings for the development of a nursing intervention protocol will be discussed.

Introduction

Preventing psychotic relapse in patients suffering from schizophrenia should be given high priority in treatment programmes for this group of patients. Optimal treatment presupposes a strategy based on a combination of antipsychotic medication and psychosocial interventions. In the past few years there has been a growing emphasis on preventing psychotic relapses by recognising the warning signs (prodromes) signalling the onset of a psychosis at an early stage. When warning signs are detected early, measures can be taken to restore the balance in a patient. Given the prolonged and intensive care provided to schizophrenic patients by nursing staff, it seems appropriate to allocate special responsibilities in this field to nurses.

This exploratory study addresses the methods of early recognition and early intervention as used in practice in six clinical settings in the Netherlands. The experiences gained with this practical use will be helpful in further intervention development. The ultimate object is to create a nursing intervention protocol that can serve as a tool for preparing relapse prevention plans with the individual patients and their social networks the purpose of which is to prevent psychotic episodes.

In chapter 4 we summarized relevant literature and we described the research methods used in this exploratory study. We described the various models used for working with relapse prevention plans as they could be constructed from our data. We explained how patients, health care professionals and other persons involved may be able to list and evaluate early warning signs systematically. Furthermore, we addressed the role of the patient's family and highlighted the beneficial effects of using early recognition and early intervention methods.

In this chapter, we will discuss the factors that influence the effective use of early recognition and early intervention methods. These factors should be taken into account in developing intervention techniques in the field of relapse prevention. The following issues will be addressed: (1) information and education, (2) attitude of health care professionals, (3) the patient's insight, (4) acceptance of illness, (5) motivation, (6) other relevant patient characteristics, and (7) continuity of care. Finally, the implications of the findings for the development of a nursing intervention protocol will be discussed.

Results

Information and Education

Health care professionals, patients and families stated that adequate information and education is essential in the context of early recognition and early intervention. In practice, information and education is offered to patients at three levels.

At the first level, general information about schizophrenia is provided. The information gives patients a general framework and appropriate terms to use in talking about their psychotic episodes. Information of this kind is offered more or less structured, depending on the setting. The issues of early recognition and early intervention are discussed in general terms; occasionally, in one of the group meetings the first steps are taken to construct a relapse prevention plan.

At the second level, the individual health care professionals provide a great deal of information and education. They can tailor the information and education to the specific characteristics of the individual patients and their environment. The relapse prevention plan is given further shape at this level, and concrete instructions are given to patients on how use the plan.

Thirdly, information and education are provided within the unit's day-to-day living environment. Everyday events are used for purposes of information and education. Suppose, for instance, that one of the patients always gets involved in conflicts about the domestic chores to be done at the unit. These conflicts cause a great deal of tension for the patient, and have already triggered two minor psychotic episodes preceded by increased feelings of anxiety and mistrust. Nurses, in collaboration with the patient concerned, can use the situation to examine how the stress-evoking chores influence the course of the patient's illness. The patient can be taught how to cope with the situation.

Many health care professional reported that a complementary package of these three forms of information clearly offers added value. It is the best way for a patient to retain the knowledge, which leads to an optimal integration of the knowledge into the patient's everyday life.

To health care professionals with experience in informing patients in group-sessions one of the advantages is that the presence and contribution of fellow patients makes it easier for the patients to make "confessions" about events and experiences during earlier psychotic episodes. The openness of others helps patients to shed their feelings of shame and they can disclose information that is important for the relapse prevention plan. One of the disadvantages, however, is that it is difficult to check whether the information provided to the group is actually absorbed and takes root. It is essential that health care professionals evaluate the effects of the group teaching and take the existing level of knowledge as a basis for subsequent interventions.

Informing a patient does not always trigger a positive response. Patients may feel that the information is forced upon them and that may cause tension and resistance, especially in situations where patients are not ready to take in information about potential future psychotic episodes. It may demoralise them. Furthermore, information may cause confusion, for instance, if a patient claims to have the early signs he hears others mention at a group meeting. This may evoke unnecessary fears of an oncoming psychosis.

Family members considered the information they obtained (usually at group meetings) as very valuable. Most of them, however, did not see early recognition and early intervention as current issues. Although they often remembered that these issues have been addressed at the meeting, their recollection was cognitive in nature and not so much aimed at any practical use. Health care professionals appear to have a task, therefore, in supporting families in translating their knowledge of early recognition into practice. Both patients and their families indicated that they needed written information - alongside the oral information - about early recognition and early intervention. This would give them an opportunity to deepen their knowledge in their own time and in accordance with their own needs.

Attitude of health care professionals

Health care professionals and families frequently referred to the attitude of the professionals and the quality of their relationship with the patients as conditions for successful early recognition and early intervention. It is important that the health care professionals develop a good co-operative relationship based on negotiation, positive reinforcement, trust and equality,

and taking the patient's experiences into account. A health care professional should be prepared to gain a thorough understanding of the patient, always responding to issues and topics that are relevant for the patient at a specific point in time. He or she should primarily focus on the patient's own "language". If a health care professional uses early recognition and early intervention predominantly as an instrumental activity, the patient will not be sufficiently motivated to apply it himself. Early recognition has the best chance if health care professionals, patients and other persons involved join forces to define how to prevent psychotic episodes in the future. Optimal co-operation can be achieved if all parties recognise this task and realise that they depend on one another to achieve the goals.

However, there are a number of obstacles to achieve this. Working with relapse prevention plans will become a problem if the health care professional assumes a patronising or blaming attitude, which the patient considers intrusive or repressive. A situation like this may occur, for instance, if a patient reports to use soft drugs. He will turn away from his counsellor if the latter responds by making rebukes. Such a response will act as a barrier to the necessary co-operation. It is better to present options to which the patient can relate. Health care professionals formulated this as follows: Convey to patients the message that we all occasionally act contrary to our interests. They added that it was important to evaluate the situation in order to help patients gain awareness of the implications, which might trigger a learning process. It is more important to preserve the patient's autonomy than to use "outside interventions" to protect him from harm at all costs, including force if need be. The latter type of intervention is often inappropriate in view of the developmental phase of the people involved in this study, most of whom were juveniles. An exception to the rule is formed by situations, which qualify as an emergency. The relapse prevention plans may sometimes mention measures, which are not accepted by patients in a crisis. If the situation is one of great urgency, the health care professionals can nonetheless impose these measures. This can put the relationship with a patient under real pressure, so it is always necessary to carefully evaluate later.

Conflicts may also arise while drawing up a relapse prevention plan. A health care worker may confront the patient with a specific behaviour in the prodromal stage of an earlier psychotic episode, whereas the patient does not recognise that behaviour as a warning sign. The patient does not interpret the behaviours as "deviant" and fails to see the use of including them in the plan.

Here, too, an open dialogue is essential and, in most cases, the patient's opinion should be decisive in the end. Health care professionals can, of course, return to the issues not accepted at a later point in time.

Another danger is that health care professionals choose their own pace in preparing the relapse prevention plan and, by doing so, rely too much on insights that the patient does not yet have and assume that the patient is motivated. It is important to see the patient's limitations. It may sometimes take months before a plan is ready and the patient regards it as workable.

Families indicated that it is important that health care professionals acknowledge the limitations of early recognition and early intervention. A psychotic episode is sometimes unavoidable, despite all efforts. In cases where health care professionals are too optimistic about the possibilities to control the process, the failure of a successful early intervention in a given situation triggers feelings of personal failure. Parents also criticised the fairly non-committal attitude with which agreements are made and put into practice. This attitude is often justified by phrases like "accept the patient as he is." A directive, non-critical attitude is necessary to ensure that patients adhere to the agreements written down in the relapse prevention plan. Interviews with the parents revealed a field of tension between the need to call
a patient to account for his actions and the need to leave a patient room for "failures" without criticising him all the time.

Insight

All interviewees agreed that a certain degree of insight into the illness is necessary to early recognition and early intervention. The analysis of the interviews revealed, however, that the concept of insight is interpreted in various ways. Some interviewees held it to be the degree in which the patient considers himself to be ill and how he qualifies the disorder. Others referred primarily to the manner in which the patient interprets his prodromes and symptoms and yet other persons related the level of insight to the patient's regularity in taking medication, especially during the pre-psychotic and the psychotic phase. Clinical impressions, such as those gained during informative sessions, formed the main source for assessing the patient's perception of the disorder. In the situations examined in this study, no objective method was used to assess people's insight into schizophrenia.

Health care professionals indicated that it is difficult to talk with patients about their disorder and the consequences if the patient's insight is low. Patients do not see any importance in discussing preventive strategies if they do not think that anything is wrong with them.

Health care professionals stated that the assessment of the patient's insight is followed up in different ways in practice. Some health care professionals regarded the lack of insight into the disorder as a reason for not working with relapse prevention plans (at least not for the time being). If a patient systematically qualifies prodromes as "non-existent" even though they are clearly visible to the outside world, the relapse prevention plan is not a viable option. Other health care professionals see a faulty understanding of the disorder as a reason to devote more time and effort to the patient, drawing up a relapse prevention plan at a pace suited to the patient and his capabilities.

Most of the patients interviewed seem to have a reasonable or good insight into their disorder. They accept that they suffer from a psychiatric disorder and need treatment. This does not mean, however, that these patients can convert their understanding into adequate action if and when required. A number of patients gave examples from the past, when they lost their perception of being ill during the prodromal phase, so that they were unable to ask for help from health care professionals. That patients can express their understanding of the disorder during remission is no guarantee for a continuing understanding during the prodromal phase. The lower the level of insight, the more a patient will have to rely on external support. A health care professional's tolerance can be tried considerably if, at a crucial point in time, a patient lacks the requisite insight into his disorder to do what has been agreed in a plan that was completed after long months of hard work.

A number of parents confirmed the loss of understanding of the disorder during the prodromal phase. The conclusion to be inferred from their answers is that these patients are well aware of the prodromes preceding a psychotic episode, but are unable to attach the right meaning to them. And if they do attach any meaning to them, there is a still a good chance that they trivialise the signs and fail to conclude that they should ask for help. Parents frequently face the situation that patients demand too much of themselves - particularly during remission - and set their expectations too high. This, too, is attributed to a lack of understanding of their own limitations. The high level of

expectations may cause a great deal of stress and evoke new psychotic episodes.

Acceptance

In their interviews, patients repeatedly made statements that indicate that they had difficulty accepting the diagnosis of schizophrenia. This failure to accept leads to feelings of gloominess, anger, resistance, denial, resignation and confusion. These feelings could change rapidly in the course of time.

Acceptance problems are mainly caused by the inability of the patients to achieve their original plans, and the observation that their peers are able to do this much better than they are. Especially the younger patients experienced problems with studying, working or maintaining relationships involving friendship or intimacy. The degree of acceptance has a great impact on the manner in which a patient undergoes treatment and the possibilities of working towards a relapse prevention plan.

Health care professionals indicated that preparing a relapse prevention plan in fact constitutes confirmation of the patient's role as a patient. Patients have to realise "… that everything was not as straightforward as it used to be." Being confronted with the need for a relapse prevention plan evokes feelings of hurt. Some patients try to retain their self-esteem by fighting the use of the plan. A response like "*you* don't walk around with a plan" confirms that the patient concerned is not prepared to accept his being part of a group of people who depend on other persons to cope in everyday life. The same applies to a reaction of strong denial: "A plan like that is fine, but I don't need it. I'm sure that it won't happen to me again."

If processes of acceptance and mourning are given too little attention, a situation may occur in which the health care professional wants to start preparing the relapse prevention plan whilst the patient is not yet ready. The patient will be inaccessible to the health care professional's ideas and there will be no basis for working towards a joint goal. According to one of the health care professionals, lack of acceptance often culminates in all sorts of passive resistance. The patient seems to respond positively to the proposal to work with a relapse prevention plan, but then fails to take the appropriate action.

A health care professional who had had quite some experience with group sessions notes that group discussions about the acceptance problems

may trigger interesting views and interactions which has an educational effect on the participants.

Motivation

There appears to be huge differences in the motivation of patients to contribute actively to early recognition and early intervention. The interviews show that many factors influence motivation. All of the issues addressed in the sections above affect the motivation of a patient in their own ways. Additional aspects that are relevant in this context are mentioned below.

Health care professionals and patients stated a number of times that the focus on early warning signs would wane in the course of time, particularly during prolonged periods of stability. Such a patient may feel that there is no longer any need to monitor his signs - by filling in score forms, for instance - and consequently may lose his motivation. Some believe that this lend support to the idea of limiting systematic monitoring to certain periods during which a patient is confronted with specific stress factors or in which he observes the very first warning signs.

Motivation may also be adversely affected if a patient is under constant pressure during his contacts with the health care system, especially during times of hospitalisation. He will be confronted with all kinds of restrictions: he is not allowed to use soft drugs, he must take medication with unpleasant side-effects, he must participate in a programme the greater part of which does not really interest him, he is awakened by a nurse who forces him to come to breakfast when he would much rather stay in bed than get up. All of this may impose such a burden on the patient that he is not motivated at all to prepare a relapse prevention plan. A health care professional commented that the patient's motivation could return all of a sudden when the pressure of his treatment was removed. It seems as if the removal creates room for the patient to work on the future.

A limited number of patients found that their right to privacy was violated, which adversely affected their motivation in the past. They do not want to disclose personal information because it makes them feel vulnerable. The feeling of being watched is particularly problematic in suspicious patients. Their parents confirmed that they had to act as "policemen" far too often and that they intruded on their children's privacy too much. The parents were somewhat ambivalent in this regard: they wished to respect the patient's

privacy and autonomy, but were also constantly aware of the dependence and need for support on the part of their child. This makes it difficult for them to deal with the child's privacy in a consistent manner.

Because of the complexity of the motivation issue, a thorough analysis of underlying causes must be conducted so as to fine-tune further interventions. It was the experience of health care professionals that relapse prevention plans had the best chance of success if the patient was motivated intrinsically to manage his situation. Motivation can be reinforced by negative experiences with previous psychotic episodes. Preventing or mitigating suffering in the future would then form a direct motivating factor. The number of psychotic episodes in the past also plays a role: the more episodes, the higher the awareness that it was not just a one-time incident.

Motivation may also be improved by the realisation, even if only partial, of the patient's plans for the future. Activities for relapse prevention can contribute to achieving targets and expectations valued by the patient within the course of his life. For instance, by increasing the level of self-management, a patient may eventually leave the hospital to go live in a sheltered housing project, an important step towards independent living.

Patient Characteristics

The health care professionals particularly mentioned a number of specific features in schizophrenic patients, which impede the use of relapse prevention plans. The presence of psychotic symptoms may cause the patient to become so preoccupied with his inner world that it is impossible for him to deal with other matters. Negative symptoms may also form an obstacle, particularly if the plan requires action. Apathy and disturbances of volition during the prodromal phase may make a patient completely dependent of others in terms of obtaining the requisite help. It appears in practice that a lack of active behaviour cannot always be clearly linked to a specific cause. Depression, cognitive deficits, resistance and laziness may also lead to inertia.

Cognitive disturbances in the fields of attention and memory will complicate the use of relapse prevention plans. It is vital for health care professionals to take these disorders into account so as to stimulate a learning process. Patients may be unable to process the information effectively and may contribute too little to turn the relapse prevention plan into an effective

tool. Functional disorders of this kind are prominent in patients with a disorganised type of schizophrenia, which makes it impossible for them to think or act in a structured fashion. A clear, structured method is essential to the process of preparing relapse prevention plans. Information must be furnished in small portions and must be repeated frequently.

The patient's personality, and the possibility of personality disorders, must also be taken into account. One of the health care professionals observed that there was a tendency to primarily consider factors directly relating to schizophrenia for early recognition purposes and to underexpose the patient's personality traits. An example concerned a patient with a negative self-image (and associated negative self-assessments) who felt himself scarcely able to gain better control of his disorder. An approach like this breeds a fatalistic attitude. For patients with anti-social personality traits, it will be difficult to set up or continue a co-operative basis for early recognition and intervention. In extremely vulnerable patients, explicit descriptions of the risk of future psychotic episodes may lead to suicidal tendencies. Paranoid patients may continuously regard their counsellors with suspicion and, as a result, have insufficient trust in them to give adequate shape to a relapse prevention plan. Some patients are - for various reasons - very reticent to share information about their experiences during the prodromal phase. Persons in their environment, therefore, cannot respond to any early sign until these manifest themselves in observable behaviour.

A patient's dependence on soft drugs or hard drugs will also influence the possibility of working with relapse prevention plans. The fact that for drug users there is always the option (to quote a health care professional) "…of overcoming lousy feelings in an easy way" sometimes makes it difficult to explore other strategies with a patient, as these will require more effort from the patient and will not have any effect until much later in time.

Finally, health care professionals reported less positive experiences involving patients with different cultural backgrounds. One of the reasons might be that these patients have different ideas about disease and mental illness, and are not so accustomed to talking about themselves or to systematically reflecting on their own behaviour. The early recognition method is indeed a product of Western beliefs and ways of thinking.

Continuity of Care

Many responses of the interviewees mentioned the concept of continuity. First of all, continuity must be provided particularly in the initial phase of preparing a relapse prevention plan. This phase is a relatively time-consuming. Given the intensive contacts between health care professionals, patients and (sometimes) their families during periods of clinical or outpatient treatment, such a setting would lend itself very well to the process of preparing the plan. This is where a major part of the basic, preparatory work required for an effective functioning of the plan can be carried out: providing information and education, writing the plan and gaining the first experience with it. A thorough follow-up phase is then required for the patient to familiarise himself with the plan and to practise monitoring his own condition. In this initial phase it is still extremely hard work to recognise warning signs and attach the correct interpretation to them. When symptoms are persistent, it is important to use systematic monitoring to define a base line in collaboration with the patient. This base line can help in making a proper assessment of the seriousness of future prodromes or symptoms.

Health care professionals and patients must constantly work on making early recognition and intervention a more or less continuous activity. The health care professionals must meet periodically to discuss how the monitoring procedures are being affected and what results they are yielding. The actual content of the plan and the question of whether it should be adjusted need to be discussed periodically. The interviews revealed that the plans are not adjusted very often to incorporate new information, so that they rapidly become out of date.

If health care professionals change too frequent, care will often focus on short-term targets. A great deal of information is lost even though it is very relevant in terms of early recognition and early intervention. A patient who had eight counsellors in only three years' time confirmed this. Because of this discontinuity, treatment and counselling becomes very fragmentary, especially when there is no proper transfer of information from one counsellor to the other. A situation like this will impede the systematic collection of data for early recognition purposes. If a treatment setting is used to take the first steps towards a system of early recognition and early intervention, it will often depend on the personal interest of the next counsellor - on coincidence, therefore - whether or not the subject is pursued later on.

Continuous care - extending beyond office hours - is essential to provide the requisite support in case of an impending crisis. Both patients and their families spoke of past situations in which they were unable to reach a health care professional or in which the professional was unavailable or unwilling to give help, even when intervention was clearly indicated. These were very discouraging experiences.

Implications for protocol development

In this article, on the basis of an exploratory study into the practice of early recognition and early intervention, we focused on a number of concepts, which obviously have a great impact on the effective use of this strategy in preventing psychotic relapse in schizophrenic patients. It is essential that these concepts are worked out in greater detail and assigned a place in developing early recognition and intervention methodology.

The study can serve as a tool to formulate a number of basic principles that must be taken into account to ensure the effective application of early recognition and early intervention:

1. The patient's own perception should serve as the point of departure.

During all stages of developing and working with the plan, the patient's perception of his world must serve as a point of departure for the activities of health care professionals. This means that they should focus on:

- the patient's everyday reality;
- the personal targets of the patient;
- the patient's developmental phase;
- the "language" of the patient.

Each situation encountered by a health care professional is unique and requires a specific approach. The desired effect cannot be achieved using standard approaches and procedures

2. The relapse prevention plan is tailor-made.

Because every situation is unique, relapse prevention plans must be made on an individual basis. In practice, this means a thorough analysis of the patient, his lifestyle and social network. The specific characteristics of the patient as well as his specific situation should be incorporated into the plan.

3. Working with relapse prevention plans is a joint activity shared by patients, health care professionals and families (or other persons closely involved).
All of these persons can contribute to the plan from their own individual backgrounds. It is always important to examine how the individual contributions might be given shape and how they can be dovetailed properly.

4.Early recognition and early intervention will have a greater chance of success if there is continuity of care.
Continuity manifests itself in:

- Continued and relatively intensive guidance in preparing the plan;
- Support to patients and their families in making consistent use of the plan and periodic evaluation of the findings;
- Continued alertness to possible adjustments on the basis of new information;
- Continuity of care through an adequate transfer of information by health care professionals in case of a change in staffing.

5. A positive appreciative attitude on the part of health care professionals is essential.
The interviews revealed that the persons involved in working with relapse prevention plans had to go through a learning process in order to apply early recognition and early intervention successfully. It has become clear that the best results in terms of learning processes can be achieved if positive appreciation is shown for the efforts made by the patients to achieve the targets set. Such an attitude proved to promote a pleasant working relationship as well. Too much emphasis on less successful aspects merely resulted in discouragement and lack of motivation.

The material produced by the studies (parts 1 & 2) can be used to outline the elements of an early recognition and early intervention method. The elements are listed in Appendix 1.
In the next research stage an intervention protocol will be developed which can be easily implemented in nursing practice. The protocol will be designed for use by nurses in their individual care of schizophrenic patients.

Appendix 1: Outlines of Early Recognition and Early Intervention Methodology

1. Preparatory Phase

- inform and educate patients and their families
- analyse the patient's situation and his social network
  concentrating on:
  - the patient's insight into the illness
  - the patient's acceptance of his disorder
  - the patient's motivation
  - specific patient characteristics, such as:
    symptomatology
    cognitive disorders
    drug dependence problems
    personality characteristics
    cultural background
  - features of social network
- decide on strategy for early recognition and early intervention
  concentrating on:
  - contributions by the persons involved (patient, family, health care professionals) to the relapse prevention plan
  - timing: have all the conditions been sufficiently achieved in the situation at hand to begin preparing the plan?

2. Listing Early Warning Signs

… listed from:

- the patient's perspective
- the family's perspective
- the perspective of the health care professional(s)

3. Monitoring Early Signs

- instruct patients and the persons directly involved on how to monitor early warning signs
- provide guidance in actual monitoring process

4. Preparing a Plan of Action

… showing as its main features:

- addresses of relevant contacts
- details of the most prominent early warning signs
- relevant sources of stress
- existing coping skills
- action to be taken by persons in the patient's immediate environment
- action to be taken by health care professional(s).

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Chapter 6

Relapse prevention in patients with schizophrenia:

The development of a nursing intervention protocol

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ACCEPTED: ARCHIVES OF PSYCHIATRIC NURSING

Abstract

This article describes the development and content of a nursing intervention protocol for the recognition of the early signs of a psychosis. By applying this protocol, nurses can contribute to the prevention of psychotic relapse in patients with schizophrenia or a related disorder. The background and construction of the intervention protocol are described. The judgment of experts in the care of schizophrenic patients on the content and applicability of the protocol is presented. Finally, the experience is summarized that has been acquired during the conduct of a number of case studies of the application of the intervention protocol.

Introduction

The prevention of psychotic relapse has high priority in the treatment of patients who suffer from schizophrenia. To achieve this goal, joint effort is needed on the part of the patient, the members of his or her social network, and professionals. Nurses can contribute in several ways to this preventive objective. They have the opportunity to offer the patient and the people in his or her environment education about schizophrenia and about its implications for daily life; they can support the patient in adequate use of medication; and, because of their regular contact with the patient, they can monitor his or her condition and take measures if his or her condition requires so. This article concerns the last possibility.

Research has shown that a psychosis in most cases arises gradually in a period from a few days to weeks (Herz & Melville 1980). Often, cognitive-perceptual changes and dysphoric symptoms first occur in the process of relapse, followed by pre-psychotic or psychotic symptoms (Birchwood & Spencer 2001). These changes in feeling, thinking, and acting that precede a psychosis are also called early warning signs or prodromal symptoms. The gradual development of a psychosis offers opportunities for preventive intervention. When early warning signs of a psychosis occur and are reported (early recognition), appropriate measures can be taken that promote the recovery of balance (early intervention).

The evaluation of the condition of the patient is an activity that is often routinely done during the contacts between the nurse and the patient. But an inventory study in the Netherlands indicated that there is a need for further systematisation of the knowledge about early recognition and early intervention (Van Mierlo 1997).

The present study attempts to respond to this need. In this article, we describe the development of a nursing intervention protocol oriented to the prevention of psychotic relapse in patients with schizophrenia.

Method

In the development of complex nursing interventions, a careful procedure should be followed. Van Meijel *et al.* (2002e) have designed a model for the development of evidence-based nursing interventions. The essence of this model is that a number of steps have to be followed for the intervention

development that have the objective of providing the building blocks for the design of the intervention. These building blocks can be assembled by means of (1) the literature, (2) analysis of the problem for which the intervention is intended, (3) research into the needs of patients and the social system and the resulting demand for care, and (4) research into already existing intervention practices. The review of the literature is an obligatory component of the process of intervention development. The use of the other research possibilities depends on the state of the knowledge and the concrete research opportunities within the intervention area concerned.

Two studies preceded the intervention development described in this article:

- A review of the literature (Van Meijel *et al.* 2002a);
- A qualitative study of present intervention practices of early recognition and early intervention in the Netherlands (Van Meijel *et al.* 2002b, 2002c). This study provides an understanding of various methods and procedures that are presently already applied. It also offers an insight into the experiences and needs of patients, family members, and care providers with these methods.

The results of these sub-studies constitute the basis for an initial design of the intervention protocol. This design was presented to eight experts in the area of schizophrenia care: two psychiatric nurses, two psychiatrists, two clinical psychologists, and two family members of schizophrenic patients. They studied the protocol and participated in a semi-structured interview. Their judgments led to further adaptation of the protocol.

The protocol was then tested in nursing practice. Four nurses who work in a university hospital and who have expert knowledge in the field of the care of schizophrenic patients received instructions on the background and the application of the protocol. Then, they applied the protocol with six patients. The first author also applied the protocol with two patients. Patient selection was done by purposive sampling, in order to have variation of the patient characteristics as regards sex, age, illness duration, treatment setting (clinic, day clinic, outpatient treatment), severity of symptoms, and level of social functioning. The nurses kept a logbook in which they noted their experiences, questions, and comments. The first author was available as a consultant for coaching the nurses while the protocol was being applied.

During the implementation of the protocol, the nurses were interviewed at two times: (1) halfway through the implementation of the protocol, that is, after the listing of early warning signs, and (2) after the protocol was completed in its entirety, i.e., when all the relevant data for the patient and the family were entered in a relapse prevention plan. The results of the case studies were used to improve the protocol.

The article is structured as follows: Firstly, we will briefly discuss the theoretical model that underlies the intervention. Secondly, we will present the structure and the procedure of the protocol, and thirdly we will summarize the judgments of the experts and describe a number of experiences from the case studies.

The theoretical model: the vulnerability-stress model

The vulnerability-stress model is a tentative model for treatment and research in the field of schizophrenia and related disorders. The model attempts to integrate the available state-of-the-art knowledge in the field of schizophrenia into a holistic perspective in which both biological and psychosocial variables have a place (Zubin & Spring 1977; Zubin *et al.* 1992; Nuechterlein & Dawson 1984; Nuechterlein *et al.* 1992; Nuechterlein *et al.* 1994; McGlashan & Hoffman 2000).

The model (see Figure 1) shows that the interaction of (1) enduring personal vulnerability factors, (2) personal protectors, (3) environmental protectors, and (4) environmental potentiators and stressors lead to "intermediate internal states". Information-processing overload, tonic autonomic hyperactivitation, and deficient processing of social stimuli here characterize the condition of the patient. These intermediate states can, when they exceed a certain threshold of gravity, lead to the development of "prodromal symptoms". They can be the precursors of a psychotic relapse. The feedback loops reflect the circularity of the model.

The model is excellently suited for the development of psychosocial interventions (Yank et al., 1993) because it makes the variables visible on which these interventions can be carried out. In the description of the intervention, we will refer to this model.

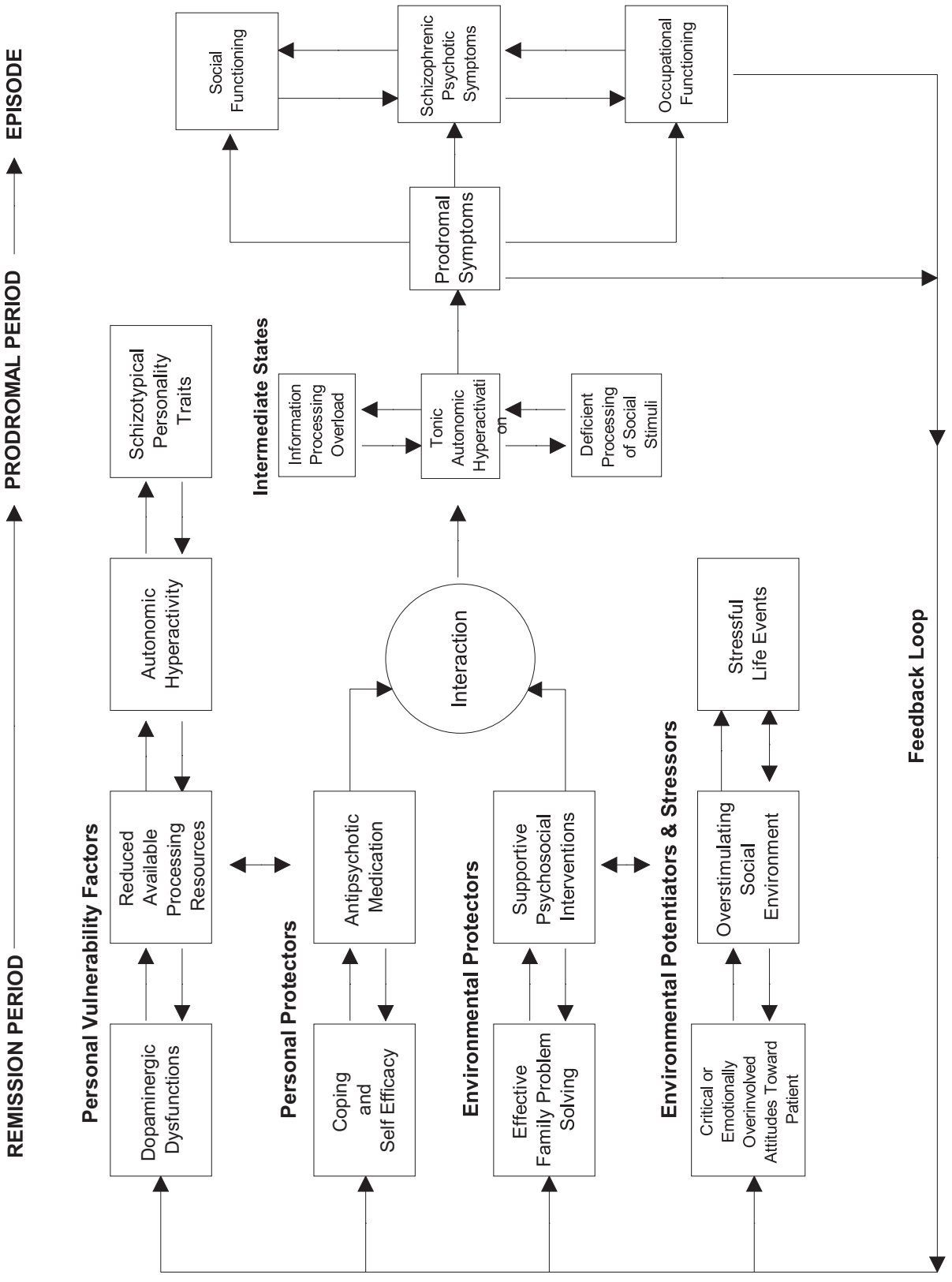

Figure 1: The Vulnerabillity – stress – model
(Printed with permission from K.H. Nuechterlein)

The intervention protocol: structure and procedure

In this section, the main lines of the structure and procedure of the protocol are described. The review of the literature and the qualitative study constitute the basis for the development of the intervention. Firstly, a number of basic principles of the protocol are described. Secondly, the various phases in the intervention protocol are explained: (1) the preparatory phase, (2) the listing of early warning signs, (3) the monitoring phase, and (4) the action plan.

Basic principles

For the application of the intervention, five basic principles have been formulated:

(1) The experiential world of the patient is the starting point:

The population of schizophrenic patients is very heterogeneous, as is the way of experiencing schizophrenia. The assumption is that starting with the actual life situation and the subjective experience of the patient results in a greater effectiveness of the intervention. This means in practice that starting with the everyday reality as it is experienced by the patient, with the goals that the patient sets for himself or herself, with the developmental phase in which the patient is situated, and with the personal wording of the patient. With this, justice is done to the uniqueness of each individual and of each life situation.

(2) The relapse prevention plan is tailor-made:

Precisely because of the unique character of each situation, it is necessary to prepare an individual relapse prevention plan. In order to do justice to this individual approach, one must carefully assess the characteristics of the individual patient and of his or her social network. With this, insight can be obtained into factors that can promote or hinder working with a symptom recognition plan in that specific situation. With this understanding, an individualized intervention strategy can be established in function of the factors described (see the preparatory phase).

(3) Working with a relapse prevention plan is (if possible) a joint activity of the patient, the care providers, and the members of the social network:

The literature and the qualitative preliminary study show that the collaboration within this triad can have considerable benefit for the preparation of the relapse prevention plan, for early recognition of the warning signs, as well as for early intervention.

(4) The relapse prevention plan continually needs adjustment:

In the course of time, new insights can arise about the early warning signs and about the things that can be done within the framework of early intervention. The learning yield can be increased for all parties by the constant translation of these new insights into the relapse prevention plan. In this way, the chance becomes greater that the relapse prevention plan will receive continuous attention within nursing care.

(5) The care provider manifests positive appreciation:

With early recognition and early intervention, the emphasis is on the increase of control over the course of the illness and over the consequences it has for the life of the patient and of the people in his or her environment. This objective will be achieved by trial and error. The motivation to learn is increased when the care provider expresses appreciation for the efforts made by the patient and others involved in order to develop a relapse prevention plan and to apply it in the patient's own life situation.

The preparatory phase

The preparatory phase starts with the introduction of the theme "working with a relapse prevention plan" to the patient and the members of his or her social network. The objective of this introduction is engagement. Firstly, one looks for the relevance of early recognition and early intervention for the patient and the social network. What positive effects can working with a relapse prevention plan have for the patient and for the people in his or her environment? The effects to which importance is attached vary widely among patients: one patient will define the desired effects in terms of anxiety reduction with regard to future psychoses, another will be interested in the contribution it makes to rehabilitation goals (for example, living independently or being employed). By the search for the personal meaning to the patient, the intrinsic motivation is increased to make an effort in early recognition and early intervention. In addition, it is important to provide factual information: What

does early recognition and early intervention actually mean? What steps have to be taken to draw up a relapse prevention plan? What is expected from the patient and, perhaps, from the members of the social network? How much time will it take? For adequate information transfer and motivating to cooperation, more than one conversation may be needed.

The next step in the preparatory phase consists of describing and analysing a number of characteristics of the patient and the social network that were found in the preliminary qualitative study to influence effective working with a relapse prevention plan. They are divided into patient-related and network-related characteristics. The patient-related characteristics are:

1. Motivation: The patient, the care provider, and the members of the social network are asked for an assessment of the motivation of the patient to make an active contribution to working with a relapse prevention plan. If the motivation is low, one looks for causes and ways to influence them.
2. Insight into the illness: the level of insight is a factor for the degree in which and the manner in which the patient will collaborate with the treatment. It also influences the capacity of the patient to reflect on his or her own psychological functioning. Insight is a complex and multidimensional notion (David 1990; McEvoy *et al.* 1989a; McEvoy *et al.* 1989b; Amador *et al.* 1993). In the intervention protocol, these dimensions are translated into a number of sub-questions that together lead to an assessment of the insight into the illness of the patient. These sub-questions concern the awareness of being psychiatrically ill, the interpretation of the psychotic experiences, the recognition of the need for treatment, adherence to treatment, and the recognition of the risk of psychotic relapse.
3. Illness acceptance: the care provider is asked to judge whether the patient has emotional reactions related to serious acceptance problems as regards the illness (and its effects) that could hinder working on the relapse prevention plan at the time. If this is the case, one may decide to postpone the preparation of the relapse prevention plan for a while and give priority in the assistance to the acceptance problems.
4. The nature and severity of the symptoms: a judgment is made of a number of positive, negative, and cognitive symptoms that could hinder the preparation of and working with the relapse prevention plan.
5. Finally, a residual category is given of influential individual characteristics, such as personality characteristics of the patient, the skill

levels (for example, in coping and problem solving), the intelligence level, addiction problems, and cultural background.

In the description of the social network, the nurse is asked to examine three aspects:

1. The extent of the social network.
2. The readiness and the actual capabilities of the members to participate in working with a relapse prevention plan.
3. Any special characteristics of the network, such as the level of expressed emotion.

The description and analysis of the patient-related and the network-related characteristics can lead to the conclusion that a number of obstructing factors are susceptible to change and others not (or to a lesser degree). The nurse is encouraged to formulate concrete steps for those factors that are changeable in the relatively short term and so can facilitate the preparation of a relapse prevention plan.

The last component of the preparatory phase consists of the "strategy determination". Here, two questions are posed:

1. Is this the proper time to begin the preparation of the relapse prevention plan? Postponement can be considered when, for example, the level of positive symptoms is still too high or when more attention must first be paid to the acceptance problems.
2. To what extent is the patient capable of contributing himself or herself to the preparation of and the working with a relapse prevention plan and to what extent is support of other people required? The information from this preparatory phase can be used to determine the need for support in divergent areas. What is important is to keep the patient from being over or under questioned and to see to it that optimal use is made of the capacities of the patient and the supporting capabilities of people in his or her surroundings.

The listing of early warning signs

The objective of this phase is the description of the most important early warning signs. In one or more discussions with the patient and, if possible,

with members of the social network, a reconstruction is made of previous relapses.

A psychotic episode that the patient can remember well is selected for discussion. The reconstruction starts with the very first changes in feeling, behaviour, and thinking that were evidence of an impending relapse. Step by step, the nurse and the patient try to describe the further course of the relapse process as precisely as possible. The capacity and the needs of the patient determine the depth to which this often-difficult period is his or her life is discussed. Additional information from members of the social network and from care providers can be valuable for completing the relapse prevention plan, certainly when it concerns warning signs, which are less well perceived by the patient or which he or she does not interpret as warning signs. The intervention protocol has a checklist of a number of common early warning signs. This list can be useful in compiling the inventory of early warning signs. All of the information together ultimately leads to an individual profile of at most the five most important early warning signs, a 'relapse signature', as Birchwood (1992) calls it. When the persons involved cannot agree on the ranking of the early warning signs, the patient decides. Indeed, the presumption is that the patient is the 'owner' of the plan and that he or she has to be able to concur with its content.

Then, the individual warning signs are worked out further as one single indication of an early warning sign is often insufficient to allow working with it. The distinction must be made between the normal/stable situation (the "baseline") and the abnormalities in comparison to this situation. For this, each early warning sign is worked out on two or three levels:

Level 1 gives the normal or stable situation; Level 2 gives a description of the warning sign when it is present in its light or moderate form; Level 3 gives the situation when it is present to a serious degree. The descriptions are prepared as concretely as possible and in the words of the patient in order to make them easier to recognize. An example of the early warning sign "increasing suspicion" can serve as an illustration:

Level 1: normal/stable

> "Regularly (almost daily) I think that people talk and gossip about me. I can succeed in dismissing these thoughts."

Level 2: light/moderate

"I think constantly that others have got it in for me. I regularly tell others that they should leave me alone and that I don't want them gossiping about me. I withdraw a lot, and I spend a lot of time alone in my room."

Level 3: serious

"I have serious quarrels with others because I think that they want to hurt me. I abuse and I sometimes hit people."

The monitoring

The monitor the early warning signs, an evaluation is made periodically of their presence or absence. The presence indicates an increased risk of a psychotic relapse, and specific actions may be appropriate to keep the condition of the patient from deteriorating. These actions are described in the action plan (see the following section).

In the preparatory phase, the need for patient support has been specified in the relapse prevention plan. The nurse can now use this knowledge to instruct the patient and perhaps also the members of the social network as regards monitoring. Concrete agreements are made about who contributes what to the monitoring.

Certainly shortly after the completion of the relapse prevention plan, monitoring should be done very regularly – preferably weekly – under the guidance of the nurse. In this way, the patient and the involved members of the social network gradually can ever more easily internalise the early warning signs. Afterwards, the frequency of the monitoring can vary more in the course of time. The qualitative study showed that weekly monitoring is *not* considered desirable and necessary for many patients. Agreements must be made with the patient and the members of the social network involved about a feasible intensity of the monitoring. Monitoring may be intensified in specific periods, for example, in times of increased stress, in periods in which medications are being changed, or in periods in which early warning signs are already present.
The monitoring is done by scoring the level of presence of early warning signs on a specially designed score form.

The action plan

The objective of the action plan is the systematic description of actions that can be taken by the patient himself or herself, by members of the social network, and by care providers in order to prevent a threatening psychosis. The point of departure is that the patient and the members of the social network always inform the nurse or psychiatrist when early warning signs occur. Together, the gravity of the situation is assessed and a decision is made about what must be done to restore equilibrium. Thus, the patient has to have someone to report to 24 hours a day to be able to commence this consultation. The 24-hour availability is the first point that is established in the action plan.

The components of the vulnerability-stress model are recognizable in the structure of the action plan. With account being taken of the vulnerability of the patient, ways are sought to avoid stress, to promote coping, and to bring about protection from the environment. In order to clearly assign the responsibilities with respect to the action plan, the actions are formulated in succession for the patient, for the members of the social network, and for the care provider.

First of all, an inventory is drawn up with the patient of the stressful situations that have to be avoided when a relapse threatens. A retrospective evaluation is made of situations that yielded much stress in the past. At the same time, one assesses which stress-inducing situations are expected in the near future. The distinction is here made between external stressors in the environment of the patient (for example, a crowded place with many people and much noise) and internal stressors (for example, the patient is frequently placing major obligations on himself or herself).

Then an inventory is drawn up of active coping strategies that can support the patient in the recovery of equilibrium. These are also strategies that were successful in the past or strategies that may be expected to be successful in the future. One may consider here relaxing activities or the application of cognitive techniques (for example, self-reassurance). Medication adherence is a standard aspect in the relapse prevention plan. Although it cannot be expected that all of the patients will simply comply with this, it can always be discussed by making it explicit in the plan. In this way, it will be clear what the patient thinks about it.

The third component of the action plan is making an inventory of activities that family members or others directly involved can engage in and that contribute to the protection and the recovery of the equilibrium of the

patient. In the preparatory phase, an evaluation is made of the capability of the social network. The nurse can use this knowledge in testing the reality content of the proposed activities. In other words, can one expect that the proposed activities can actually be carried out and lead to support and protection and thus to recovery of equilibrium? In addition, what certainly should *not* be done by people in the patient's environment because it increases the stress for the patient is discussed with those involved. For example, one may consider all kinds of concrete behaviour that lead to an increased level of expressed emotion, with the most important characteristics being emotional *over*-involvement, critical statements, and hostility because of the behaviour of the patient.

Finally, the actions of the care provider are formulated. Three types of actions are distinguished here:

(1) Actions that the care provider formulates from his or her own professional expertise (for example, promoting medication compliance),
(2) Actions at the request of the patient (for example, contacting the employer to explain the condition of the patient),
(3) Actions at the request of family members and other people involved (for example, more intensive telephone contact with the parents of the patient to keep them informed of the treatment policy and the way in which they can contribute to this policy).

After description of all the relevant data in the relapse prevention plan, it is determined in consultation with the patient who should receive a copy of it. Generally, this is done in line with previous agreements on the involvement of various people in the compilation of the relapse prevention plan. The people who are involved only in a late stage in the relapse prevention plan receive information and instruction about the plan with explicit attention to their specific contribution to the preventive strategy.

The judgment of experts

The interviews with the six experts in schizophrenia care produced statements on two different levels.

First, there were the statements on the various details of the intervention protocol. They often concerned formulations, additions, qualifications, and the

like. They were evaluated by the authors and have been incorporated in a subsequent version of the protocol if they were considered able to improve the interventions.

Second, statements were made that were of a more comprehensive nature. We summarize the basic ideas here.

The experts evaluated the manner in which content was given to the intervention protocol predominantly positively. The central place assigned to the perspective of the patient and of the family was seen to be an important success factor. The experts also appreciated the opportunities the protocol offers for individualization. In their judgment, a good balance was found between structure and individual customized work. The structure is important to give the parties a grip when executing the intervention, while the customized portion is necessary to have the intervention be in line with the individual situation of the patient and the members of the social network, as well as with the organizational context within which care is provided.

Several experts stressed that the success of the application of the intervention depends largely on the level of competence of the nurse. The protocol is partially prescriptive, but also, for another part, requires adaptation of the intervention strategy to the understanding present, such as the understanding acquired in the preparatory phase of the protocol. This working on the basis of understanding places relatively high demands on the ability of the nurse to carry out abstract clinical reasoning and clinical decision-making. It also makes high demands on the communication skills of the nurse to share considerations, if necessary and desirable, with the patient and the family in order to come to joint decisions. In addition, the implementation of the protocol makes high demands on the organizational ability of the nurse. The intervention can lead to success only if the nurse is the central person responsible for the execution of the care. Here, the imbedding of the relapse prevention plan within the multidisciplinary collaboration and the synchronization with the total treatment plan was cited as particularly important.

Several experts offered critical comments on the length of the intervention protocol and its consequences for the implementation opportunities. Their fear was that the comprehensiveness in combination with the extensive substructure of the various components would be at the cost of the readiness of nurses to actually implement the protocol. In view of the consistency with which the experts expressed this observation, a more concise version of the intervention protocol was designed (the work protocol). In organization and structure, this

version corresponds with the original protocol, but most of the explanatory information has been removed with a view to practical manageability. The original protocol was used in the subsequent research (see chapters 7 & 8) primarily for educational purposes and as a reference work for the protocol users.

The case studies

The nurses who participated in the case studies also offered critical observations as regards the practical manageability and the implementation of the protocol. The need for a more concise version of the protocol was stressed. At the same time, the need for more intensive instruction was expressed, in which the emphasis should be placed primarily on practical examples and on the question of how one should deal with an obstinate practice in which the preparation of the relapse prevention plan proceeds in a much less orderly manner than described in the intervention protocol. Particularly the reconstruction of earlier psychoses, the selection of the most characteristic warning signs, and the elaboration in three levels of severity (with sufficient internal consistency and discriminatory power) were seen to be difficult in a number of cases.

The experience of nurses was that implementation of the intervention protocol contributed a great deal to the ordering of the information already available. But it also provided much new information. For example, one of the nurses, by implementing the protocol, realized the cognitive limitations of the patient and in particular the memory problems that made the execution of tasks and compliance with agreements difficult. Another nurse got to talk to the patient about the persisting symptoms and the way in which they had an effect on everyday life. And again another nurse learned about a hitherto unexpressed intense anxiety on the part of the patient for a new psychosis, an anxiety that was fed by statements of the attending physician in that regard.

Also important was that the experiential aspects of earlier psychoses were discussed. The respondents noted that it must sometimes be very strange for patients that such a major life-event as a psychosis is discussed so little with care providers. For a number of patients, experiences from previous psychotic episodes were discussed productively during the compilation of the relapse prevention plan. But there is also the risk of upset, as appeared in one case. Old conflicts with the partner were revived when previous psychotic episodes

were discussed, and a strict structuring turned out to be necessary to limit the upset for both the patient and the partner.

In the execution of the case studies, a great deal of empirical support was found for the individualization aspect. This appeared already from the tempo of execution of the intervention. For one patient, a very detailed relapse prevention plan could be drawn up within four weeks because the patient manifested a great deal of insight into the illness and readiness to work to prevent future psychoses. She very diligently and with great self-sufficiency did her homework. For another patient, this process took so long that it could not be completed within the research period. The capacities of this patient were significantly less. The preparations for transfer to sheltered housing and an increase of psychotic symptoms led to a delay of a number of months. Another patient could not take in the information on early recognition and early intervention because she was preoccupied with obsessions that took all her attention. This same patient also was afraid to write things down on paper. She was afraid that she would thus become too "transparent". It required much diplomacy to collect the necessary information without destroying the willingness of the patient to cooperate.

Again another patient objected to the word "psychosis". She had "spiritual experiences", and only with this wording the dialog could proceed about preventive measures that could contribute to her stability. With several patients, it was a matter of running the gauntlet periodically in order not to overburden them and to maintain collaboration for the preparation of the relapse prevention plan. Also the participation of family or other members of the social network needed individualized trajectories and using these contributed to the success of the intervention.

In several cases, the relapse prevention plan turned out ultimately to be a very good means of communication for making explicit agreements about the involvement of various people in care delivery. From the perspective of the patient, this meant the organization of social support and protection as well as the prevention of stress – for example, in the form of a high level of expressed emotion. From the perspective of the family, this meant clarity regarding the question of the role they could play in the care of the patient and also clarity about when they could leave the care to others.

Conclusion

This article describes the construction and preliminary testing of a nursing intervention protocol directed to the prevention of psychotic relapse in patients with schizophrenia. An attempt is made to integrate the perspectives of the patient, the family members, and the care providers within the procedure of the protocol in order to achieve optimal collaboration in the prevention of psychosis. The experiences of patients and family members occupy an important place within the proposed procedure. The expectation is that the readiness to use the protocol and the effectiveness of the intervention increases with the degree in which account is taken of these experiences. In the protocol, the rationale for the various sub-interventions is made explicit, which makes it possible for the nurse to deviate with reasons from the protocol when the concrete situation requires it. The case studies made it clear that a different strategy was used in each case to arrive at a relapse prevention plan, depending divergent factors related to the patient, the social network, and the care context. It also became clear that the ideal circumstances are almost never present. The best possible strategy always has to be chosen within the existing possibilities and restrictions, which can vary considerably over time. It requires a high level of competence of the nurse to deal flexibly and creatively with these possibilities and restrictions.

Our experience is that working with protocols in general is not particularly popular among care providers. Perhaps, this is because they rapidly get the impression that too much is prescribed and that the opportunities for self-determination within the care process are being curtailed. The case studies showed that the emphasis on individualization of the method was highly appreciated by the nurses. We expect this to increase the readiness to integrate the proposed strategy of early recognition and early intervention in the care that nurses offer to patients with schizophrenia.

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Chapter 7

Relapse prevention in patients with schizophrenia:

The application of an intervention protocol in nursing practice

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-SUBMITTED -

Abstract

This article describes the results of a survey conducted among nurses who work in psychiatric care. Within the experimental condition of a randomised controlled trial, they executed an intervention protocol to prevent psychotic relapses among schizophrenic patients. The central objective of this protocol was early recognition of the warning signs of psychosis and timely performance of actions intended to re-establish the equilibrium of the patient.

The nurses were asked about the execution of the intervention, their experiences with it, and their evaluation. The nurses actually did execute the protocol in large measure and also made use of opportunities to tailor it to the individual patient. For the most part, the nurses judged that the intervention protocol contributed significantly to the treatment of the patient. The survey also revealed a number of difficulties in the execution of the protocol that deserve attention in the future.

Introduction

The development and testing of evidence-based interventions in health care have attracted increasing attention in recent years, in part because of the need to provide high-quality and effective care that contributes demonstrably to health benefits for the patient. The scarce resources available for health care must be used cost-effectively, which means maximum yield at an acceptable cost.

In nursing too, evidence-based practice is necessary. Nurses are trying to specify what they do or should be able to do in the form of nursing interventions that can then be examined for its effectiveness and efficiency. The present study is seen to be in line with this development.

The research project of which the present study is a part is focused on the development and testing of a nursing intervention protocol geared to the prevention of psychotic relapses in patients with schizophrenia and related disorders. It was developed on the basis of a review of the literature (Van Meijel *et al.* 2002a) and qualitative research (Van Meijel *et al.* 2002b/c). The effects of the application of the protocol are investigated in a randomised controlled trial (RCT) with the occurrence of psychotic relapses and re-hospitalisation being the most important measures of outcome (see chapter 8).

This article presents the results of a survey conducted among nurses who applied the protocol within the experimental condition of the RCT. The objective was to obtain an understanding of the manner in which the protocol was actually used in the RCT and of the experiences and evaluation of the nurses with it.

The intervention protocol

The protocol is intended for patients who are diagnosed as having schizophrenia, schizophreniform disorder, or schizoaffective disorder (APA 2000). The intervention protocol (Van Meijel *et al.* 2000; Van Meijel *et al.* 2002d) instructs nurses in how to draw up, together with these patients and members of their social network, a relapse prevention plan in function of the individual situation and how they can then work with it.

The relapse prevention plan contains a detailed description of early warning signs of a psychosis: changes in feelings, thoughts, and behaviour of the patient that can be considered early warning signs of an impending

psychosis on the basis of previous experience (Heinrichs & Carpenter 1985; Herz & Melville 1980). When these signs are noted in an early stage (early recognition), one can intervene preventively (early intervention) in order to contribute to the recovery of the equilibrium of the patient. The preventive actions are listed in an action plan, which is part of the relapse prevention plan. The intervention protocol consists of four phases:

(1) The preparatory phase;
(2) The listing of early warning signs;
(3) The monitoring of the early signs;
(4) The preparation of an action plan.

The intervention protocol is so devised that the nurses are offered a good deal of structure in the execution of the intervention but still sufficient space for adapting the method to the individual characteristics of the patient, of the members of the patient's social network, and of the specific context within which care is provided.

Methods

The present study was conducted during the RCT in which the effects of the intervention were examined. The nurses in the experimental condition received instruction in the application of the intervention protocol. They then executed the protocol with one or more patients. The nurses in the control group offered 'care as usual'. In a follow-up period of 1 year, the psychotic relapses and re-hospitalisations were noted. The central research question within the RCT was whether the patients in the experimental group had fewer psychotic relapses and needed fewer readmissions than did the patients in the control group.

When the relapse prevention plan was ready in the experimental condition and the follow-up year could start, the nurses were given a survey form. A number of questions and statements about the execution of the interventions were presented. Three research questions were central:

- How did the nurses actually execute the intervention protocol?
- How did the nurses experience working with the intervention protocol?
- What value do the nurses assign to the execution of the intervention protocol?

The responses to these questions are important for an understanding of the process of the execution of the intervention. The results of the RCT can then be related to the results of the process study.

The structure of the intervention protocol was mirrored in the design of the survey. Structured questions were used to determine the actual application of the intervention by the nurses. Open questions offered the opportunity to make qualitative comments. In addition, positively and negatively formulated statements were presented to obtain an understanding of the experiences of the nurses with the intervention protocol and the value they assign to the intervention. Finally, in the last part of the survey, a number of statements were presented in order to gauge the appreciation of the nurses of the intervention protocol as a whole. A 5-point Likert scale ranging from "strongly agree" to "strongly disagree" was used for the scoring.

The instructions for the survey emphasized that there were no "correct" or "incorrect" answers in order to reduce the tendency to give socially desirable replies. It was stressed that the intervention protocol had to be adapted to the specific characteristics of the patient, the social network, and the social context. This inevitably leads to divergent methods. The nurses were thus encouraged to report on the actual method used, to describe the experiences encountered, and to make an evaluation.

Fifty-one stabilized patients were included in the experimental condition of the study. Thirty-six of them were receiving outpatient care, six were in day care, and nine were hospitalised. Eleven patients dropped out for various reasons during the preparation of the relapse prevention plan: early discharge of the patient (n = 1), the stress caused by the preparation of the relapse prevention plan (n = 2), psychotic relapse (n = 1), lack of motivation (n = 5), and lack of time on the part of the nurse (n = 2).

Ultimately, a complete relapse prevention plan was prepared with 40 patients involving 26 nurses. Of the 40 survey forms, 35 were returned. Two forms were not returned because the nurse was on sick leave, and the other three were simply never returned with no reason given, in spite of repeated reminders.

The data were entered in an SPSS database and analysed with descriptive techniques.

Results

The results are given for each phase of the intervention protocol and then the total protocol will be evaluated.

A. The preparatory phase

The results are discussed in function of the four-part objective of the introductory phase.

(1) The introduction of the theme "working with a relapse prevention plan" with the patient and with members of the social network:

Before a relapse prevention plan can be prepared, an introduction to "working with a relapse prevention plan" is required for the patient and, if appropriate, for the members of the social network. The objective is to provide information, to create a basis for collaboration, and to make concrete agreements about the involvement of various people in the preparation of the plan.

All of the nurses conducted one or more introductory discussions with the patient and, if appropriate, the members of the social network. In half of the cases, this introductory discussion was held only with the patient; in the other half, one or more members of the social network were also involved.

In 85% of the cases, concrete agreements were made about the involvement of members of the social network in the preparation of, and working with the relapse prevention plan. In most of the cases (57%), one opted to invite network members a number of times during the preparation of the plan in order to inform them of the progress and to exchange information about the relapse prevention plan. In two of the 30 cases, an even more intensive form was chosen whereby members of the social network were permanently present during the preparation of the plan.

Some of the patients, however, opted for less intensive involvement of their social network. A fourth of them considered it sufficient that members of the social network be informed about the content of the relapse prevention plan after it was completed. Ten percent of the patients wanted no involvement at all of outsiders. For them, the relapse prevention plan was a matter between themselves and the nurses.

Virtually all of the nurses (94%) considered the introductory discussions with the patient to be an important or very important part of the protocol in

order to achieve good cooperation in the preparation of a relapse prevention plan. This judgment applied to a somewhat lesser degree to the introductory discussions with members of the social network (77%).

(2) The description and analysis of the characteristics of the patient and the social network relevant to working effectively with a relapse prevention plan:

From the qualitative preliminary research, carried out in context of the broader study, a number of patient- and network-related factors emerged that appeared to influence the possibility of working effectively with a relapse prevention plan. These factors were worked out in the intervention protocol in order to assess the degree in which they inhibit or promote the application of the intervention protocol. The intention was for the nurse to use this information to adapt the intervention to the individual patient with the expectation that such an individualized method would enhance its effectiveness.

The primary patient-related factors are the patient's motivation, insight into the illness, and acceptance of the illness and the nature and severity of the symptoms. In virtually all of the cases, the nurses evaluated these factors according to the protocol.

The network-related factors were the size of the social network, the readiness of its members to participate in working with the relapse prevention plan, and individual characteristics of the social network (for example, a high level of expressed emotion). These aspects received somewhat less attention in the preparation and were actually evaluated in 68 to 83% of the cases.

The nurses confirmed that the assessment of the patient-related factors was important or very important for the preparation of the relapse prevention plan. The value of the assessment of the network-related factors was judged less univocally. In 70% of the cases, the information received was considered valuable for the preparation of the relapse prevention plan.

(3) The performance of actions to create favourable conditions for working with a relapse prevention plan:

A number of the factors indicated above can be influenced by focused actions in order to create more favourable conditions for working effectively with the relapse prevention plan. In 31% to 46% of the cases, actions were actually formulated with respect to the various factors. The survey does not provide information on the precise nature of these actions or on the degree to which they really did lead to more favourable conditions. The value of the formulation of these actions is that the nurses did not simply accept the

limitations encountered as given, but instead took steps to influence them to enhance the intervention.

(4) The determination of a strategy for the preparation of and working with a relapse prevention plan:

The determination of the strategy is intended first of all to establish whether, on the basis of the available information, the present is the proper time to start the preparation of the relapse prevention plan or whether it would be better to wait for a while. This would be the case, for example, if the patient still manifested too many psychotic symptoms or if other treatment objectives had a higher priority at the time. For a fifth of the cases, there were reasons to postpone the preparation of the relapse prevention plan.

The second part of the determination of the strategy consisted of judging the degree to which the patient could contribute actively to the plan and, complementarily, the amount of dependence on others in the process. The results of the survey indicate that almost half of the patients who participated in this study were able to contribute actively to the preparation of the plan with the dependence on others being low. A somewhat smaller portion (40%), was moderately dependent on others because of limitations and handicaps that required support in one or several areas in order to obtain a usable relapse prevention plan and subsequently to be able to work adequately with it. In 10% of the cases, the restrictions and handicaps were so substantial that the dependence on others was judged by the nurses to be very great.

A good 90% of the nurses indicated that they considered this "determination of strategy" to be an important or very important part of the intervention protocol.

B. The listing of early signs

In this phase of the intervention protocol, the nurse, the patient and members of the social network looked back at previous psychotic relapses. Together, a judgment was made about what the most important early signs were during these previous relapses. The assumption is that certain of those early signs would also occur in the future in the early phase of a psychosis. Their early recognition would make early intervention possible. In order to enhance clarity, the intervention protocol instructed the nurse to select a maximum of five signs. These signs were then classified into three levels of severity.

It would thus become clear when the situation is normal and when there would be reason for concern and for undertaking action.

A wide range of information sources can be used in inventorying these early signs, and using several sources can increase the validity of the inventory. All of the nurses in the study made use of information provided by the patient about experiences during previous relapses and supplemented it with information from members of the social network. The nurses differed in their judgments about the relative importance of this latter information. In half of the cases, the nurses considered the information from network members to be so important that a good inventory of the early signs could not have been made without them. In the other half, the information from network members was considered less critical and more of a supplementary nature.

The observations of the nurses themselves during previous relapses were also an important source of information and could be used in 90% of the cases in the listing of the early signs. Information from medical or nursing records was used to a lesser extent, in 40% of the cases.

The intervention protocol provides in appendix a checklist of common early signs. This list was derived from an existing measurement instrument for the scoring of early signs of a psychosis, the Early Signs Scale developed by Birchwood *et al*. (1989). It was assumed that this checklist would be superfluous in most of the cases because most patients and network members would be able to compile enough information about the most characteristic early signs in the context of an open interview. Nevertheless, all but two of the nurses used it, so the list apparently has more practical value than was originally assumed. This was also confirmed by the judgment of the nurses: 85% of the users considered the checklist to be an important aid in listing the early signs.

In the qualitative preliminary study preceding the formulation of the intervention protocol, working with homework assignments seemed to be a good option for some of the patients: the initial impetus for the identification and working out of early signs could then be given by the nurse and the listing could be worked out further by the patient with the support of network members if need be. Almost half of the patients listed early signs as homework assignments.

A good three quarters of the nurses indicated that the most important early signs of an individual patient could be listed rather easily, and consensus

was reached among the patient, the members of the social network, and the nurse about the most important early signs in almost all of the cases. The interview strategy proposed in the protocol with the possible use of the checklist of early signs in combination with consultation of the patient's records was apparently sufficient for most cases. In situations in which this generated more problems, the nurses ultimately succeeded in completing the inventory.

Not all elements of this phase proceeded as easily. The working out of three levels of severity proved to be more difficult. Almost half of the nurses found it difficult to achieve this.

It is also important at this point to consider the question of the extent to which talking about previous psychotic relapses might be too burdensome to the patient. From the data in the qualitative preliminary study, it was inferred that this confrontation could be too demanding for some of the patients and that the accompanying stress might even induce psychotic symptoms. Two thirds of the nurses reported that the patient had found it disturbing to have to think about previous psychotic crises. In 20% of the cases, this subjective burden had real adverse consequences. In these cases, the nurses considered that talking about previous crises caused serious distress.

Members of the social network experienced the discussion of previous psychotic crises less of a burden. However, in the opinion of the nurses talking about previous psychotic crises imposed a considerable burden on the network members in a fourth of the cases.

The question, finally, is whether the listing and working out of early signs actually do yield more knowledge and insight. This certainly is true for the nurses: three quarters of them reported having acquired new knowledge about the patient. In the judgment of the nurses, half of the patients and members of the social network also acquired new knowledge.

C. Monitoring early signs

In this phase, the nurse monitors possible early signs at least once a week with the patients and, if possible, with the members of the social network. As to the number of people actively involved in the monitoring, in almost a third of the cases the monitoring remained a matter between the patient and the primary nurse. Nobody else was involved. In half of the cases, another person was involved, and in the remaining cases (20%) a fourth person also

participated in monitoring. Parents occupied a relatively important place in the monitoring, being active in 40% of the cases. To a much lesser extent, other family members (brother or sister), partners, friends, and acquaintances were involved (10 to 15%).

Periodical monitoring is crucial for effective execution of the intervention. However, from the results of the survey indicate that a third of the patients did not really see the importance of regular monitoring. The nurses expected that 70% of the patients would do the monitoring regularly, while it is still uncertain for 15% of the patients. The nurses did not expect the remaining 15% to do the monitoring.

The conclusion is that regular monitoring of early signs will require joint efforts of the patient, the network members, and the caregivers. The participating nurses considered that for 80% of the nurses weekly monitoring is feasible by the combined efforts of the people involved.

D. The action plan

In this part of the intervention protocol, the nurse, the patient, and the members of the social network together prepared an extensive action plan with the aim of contributing to the recovery of the patient's equilibrium in periods of impending relapse. Attention is given to the use of medication, the prevention of stress, the enhancement of coping, and the use of protection from the environment. Practical agreements were also made about the 24-hour availability of professional assistance.

The use of available information sources was very similar to what was seen in making the inventory of the early signs: in all of the cases, the patient himself or herself provided information for the action plan. Further, the primary nurses contributed to its content (90%), and the members of the social network were also intensively involved in three fourths of the cases.

Information from the patient's records contributed to the content of the action plan in almost 50% of the cases. A third of the patients contributed to the action plan by means of homework assignments.

A substantial number of the nurses reported that they had difficulties preparing the action plan, particularly in establishing the contributions to the action plan by people from the environment of the patient. Nurses reported this to be difficult in 55% of the cases as was the identification of coping

strategies that could be used by the patient to deal with his or her early signs (37%). To a lesser extent, this was also the case with the manner in which stressful situations could be avoided (23%) and the manner in which the caregiver could contribute to the prevention of relapse (17%).

An important component of the action plan is the 24-hour availability of the professional assistance, as it should be easy to contact the caregivers in the event of an impending crisis. However, no definite agreements could be made in this regard with a third of the patients and concerned members of the social network.

E. General evaluation

In the previous sections, we presented the way in which the different components of the intervention protocol were used and how the application of the protocol was experienced.
In this section we will address the evaluation of the protocol as a whole.

All of the nurses, with one exception, considered the preparation of the relapse prevention plan to be a meaningful activity. In their judgment, the relapse prevention plan contributes significantly to the treatment of the patient. More concretely, the relapse prevention plan was a useful instrument for the patient for controlling the course of the disorder. In two thirds of the cases, the nurses succeeded in clearly establishing the responsibilities of the patient, the nurse, the psychiatrist, and the members of the social network in times of impending crisis.

The nurses were less convinced that the patient could manage the relapse prevention plan sufficiently: in 17% of the cases, the nurse expected problems with the practical implementation of the relapse prevention plan by the patient. In an additional fourth of the cases, this could not be evaluated at the time of the survey. The answers indicate that attention should be given to supporting the patient in using the relapse prevention plan in the follow-up period.

Eighty-five percent of the nurses indicated that they were satisfied with the final relapse prevention plan. As the patients were not interviewed in this part of the study, the nurses were asked about the extent to which the preparation of the relapse prevention plan was a meaningful activity for the patient. The nurses considered that this was the case for two thirds of the

patients. Resistance to the preparation of the relapse prevention plan on the part of the patient was observed in 10% of the cases.

The intervention protocol is designed to have nurses harmonize their strategy and methods in the preparation of the relapse prevention plan with the specific characteristics and needs of the patient and the members of the social network. In this way, the result is a "tailored" plan that is expected to be the most acceptable for all the parties involved. The various components of the protocol offer an opportunity to put this individualized approach into practice. In 90% of the cases nurses consider that they succeeded in individualizing the way one worked with the intervention protocol.

Thus, the intervention protocol offers the opportunity to provide individualized education to the patient and the members of the social network about matters associated with psychosis, the risk of relapse, and the way in which relapses can be prevented. In two thirds of the cases, nurses considered that there were opportunities for psycho-education for the patient during the preparation of the relapse prevention plan. However, this was considered the case for only a third of the members of the social network.

The final question of the survey concerned the training the nurses received in preparation for the execution of the intervention protocol. A large majority was satisfied with it. Only two of the 26 participating nurses felt that the two instruction periods that had been offered were insufficient for the proper execution of the intervention protocol.

Conclusions

In general the nurses considered that the intervention contributed meaningfully and significantly to the treatment and care. The various components of the intervention protocol were implemented, and they were considered necessary in arriving at a good relapse prevention plan.

Even though the nurses followed the structure of the intervention protocol quite faithfully, they still succeeded in harmonizing their approach with the specific characteristics of the patient and of the members of the social network. Thus an important objective of the protocol was achieved, that is, the combination of structuring and standardization of the nursing action with individualization of care. It is likely that this combination enhanced the acceptance of the intervention by the nurses. Our assumption in the construction of the intervention was that the nurses would not want to have

detailed prescriptions about how to proceed in the provision of care, and that they would want sufficient room for decision making to be able to offer appropriate care on the basis of their own assessments.

We may also conclude that the patients and the members of the social network contributed significantly to the preparation and use of the relapse prevention plan. Here, too, one of the initial intentions of the protocol was realized, namely, that one would strive for as much collaboration as possible within the triad of patient, members of the social network, and professionals.

For some of the nurses the preparation of the relapse prevention plan did not turn out to be as easy as for others. Problems were reported mainly in the working out of the early signs in three levels of severity. This task is quite analytical, and choices have to be made about the way in which specific signals can be ordered in a meaningful and, for the patient, recognizable manner. This aspect should receive more emphasis in the training of the nurses.

The nurses were optimistic about the possibilities of monitoring the early signs even though the importance of regular monitoring was not realized by some of the patients and network members. Support and direction by the nurse is desirable lest they gradually begin to pay ever less attention to the relapse prevention plan.

Attention must also be given to the burden that the preparation of the relapse prevention plan involves for the patient and the members of the network. In particular, being reminded of earlier psychoses seems to be considerably burdensome for some of the patients. Dosage of the confrontation could reduce this burden.

Another area requiring attention is the 24-hour availability of professionals. In the qualitative preliminary study (Van Meijel *et al.* 2002 b/c), family members in particular expressed their frustration in trying to contact professionals when, in their judgment, such contact was urgent. The survey indicated that regarding 24-hour availability no definite arrangements were made in a third of the cases. Hence, availability has to improve.

The intervention protocol was developed in detail in previous phases of the research. An extensive review of the literature was conducted as well as a qualitative study of existing intervention practices in which experience was acquired with early recognition and early intervention. Experts evaluated draft versions of the protocol, and the intervention was tested for feasibility in nursing practice by means of case studies. Thus, the way in which the protocol was developed contributed to a product that would have high likelihood of being adequate and practicable. The positive experiences of the nurses are

certainly the result of this procedure. A careful developmental trajectory of nursing interventions increases the chance of effectiveness, and this certainly applies for relatively extensive and complex interventions that are executed within nursing practice (Van Meijel *et al.* 2002e).

In the execution of an RCT, it is important that a clear description of the intervention be available and that one determine how this intervention has actually been executed in the experimental condition. In the present study we investigated how the intervention was executed, what the experiences were of the nurses, and how the nurses evaluated the intervention. The results of this research make us optimistic about the application of the intervention protocol within nursing practice. The next obvious research question is whether working with the relapse prevention plans actually does have the intended preventive effect on the occurrence of serious psychotic relapse (see chapter 8).

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Chapter 8

Early recognition and early intervention in patients with schizophrenia: The results of an intervention study in nursing practice.

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- SUBMITTED -

Abstract

This experimental study addresses the question of whether the use of relapse prevention plans (RPPs) in nursing practice is more effective than care-as-usual in reducing relapse rates among patients with schizophrenia or a related psychotic disorder. Nurses and patients were randomly assigned to either an experimental or a control condition. Nurses who were selected for the experimental condition received training on how to use the intervention protocol in the process of drawing up an RPP with the patient and members from his/her social network. The purpose of an RPP is to recognize early warning signs of an impending relapse, to be followed by early intervention to restore the equilibrium of the patient. Following completion of the RPPs, the patients were followed for a period of 12 months in which the early warning signs were monitored regularly. The patients who participated in the control group received care-as-usual.

Patients from the experimental group (n=40) and the control group (n=42) who completed the follow-up period were comparable on baseline measurements. The relapse rates in the experimental and control groups were 12.5% and 26.2%, respectively. This difference is not statistically significant ($X^2_{(1)}$=2.445; p=.12). Survival analysis shows a comparable p-value. The relative risk (RR) of a relapse in the control group versus the experimental group was 2.095 (CI 95%: 0.79<X<5.00). No significant or interpretable differences could be discerned at the level of secondary variables such as insight, quality of the working alliance and use of anti-psychotic drugs.

In conclusion, the RR of 2.095 indicates that in this study a positive effect of the intervention was found, but the effect observed is not statistically significant.

Introduction

Schizophrenia is a psychiatric disorder that is chronic for most patients. Periods of relative stability alternate with periods in which psychotic symptoms are prominent. During these psychotic episodes, symptoms like hallucinations and delusions occur. Further, the patient's thinking is often disorganized, and he or she can manifest seriously chaotic behaviour. For the patient and for the people in his or her surroundings, psychosis is generally a great burden. The patient is anxious and confused; social relations become disturbed; the dependence on care services increases; and social recovery can last from months to years.

The prevention of psychotic relapses receives much attention in present treatment programs. On the basis of the present state of scientific knowledge, it can be stated that the combination of pharmacological therapy and psychosocial interventions is the most effective way to prevent psychoses (APA 1997). Nevertheless, it is estimated that the annual percentage of relapses under the present treatment conditions is around 40%. According to a number of authors, this percentage is unnecessarily high and every effort needs to be made to further optimise the treatment (Kissling 1991, 1992; Bellack & Mueser 1993; Ayuso-Gutierrez & Del Rio Vega 1997). The relapse percentage could be further reduced, perhaps to some 15 to 20%. Optimisation of the treatment comes down largely to stricter application of the knowledge presently available (Backer *et al.* 1986).

This article concerns a psychosocial intervention that has the objective to contribute to the prevention of psychotic relapses. The intervention consists of the early recognition of the early signs of a psychosis. These early signs are changes in the experiencing, thinking, and behaviour of the patient that occur in the preliminary phase of psychotic relapse. When the recognition of early signs is adequate, preventive measures can be taken to prevent development into a psychotic crisis.

The early signs can vary considerably from patient to patient. The assumption is that they manifest a certain consistency in a particular patient over successive psychoses. The nature of the early signs changes as the process of relapse advances. Birchwood & Spencer (2001) describe three phases that can often be recognized in the preliminary phase of a psychosis: first, there are cognitive-perceptual changes (for example, attentional dysfunction, derealisation and racing thoughts), which are followed by signs of dysphoria

(for example, low mood, fear and pre-occupation with mental life). These change gradually into pre-psychotic early signs, such as increasing suspiciousness, ideas of reference and hearing voices.

The same authors argue for the identification of a "relapse signature" for each patient, a profile of his or her most characteristic early signs. This individual profile contributes to a high predictive value of the early signs: when they occur, the chance is great that they will actually be followed by a psychotic relapse if there is no therapeutic intervention.

The expectation is that early recognition and early intervention are readily applicable within nursing care. Indeed, nurses have frequent contact with the patient and the family members and so can observe well the condition of the patient. Van Meijel *et al.* (2002b/c) studied the existing early recognition and early intervention practices in the Netherlands. These practices involved the preparation of relapse prevention plans in conjunction with the patient and members of his or her social network. This plan includes the early signs of the patient that were worked out as well as the actions that could be taken when psychotic relapse threatens. The results from this study, in combination with the results of a review of the literature (Van Meijel *et al.* 2002a), were used to devise an intervention protocol for the preparation of relapse prevention plans with schizophrenic patients in nursing practice. In the design phase, the intervention was evaluated by experts and by means of a number of case studies (Van Meijel *et al.* 2002d). The definitive version of the protocol was then established.

In the present article, we describe the research into the effectiveness of the intervention protocol. The research question is as follows:

> *"Do patients with schizophrenia and related psychotic disorders with whom the relapse prevention plans are applied have less chance of undergoing a psychotic relapse than do patients who receive care-as-usual?"*

Secondarily, we study the effects of working with relapse prevention plans on (1) the insight of the patient into the illness, (2) the working alliance between the patient and the nurse, and (3) the use of medication.

Description of the intervention

The intervention protocol gives step-by step instructions to the nurse on how he or she can systematically prepare a relapse prevention plan with the patient and with members of the patient's social network. (Van Meijel *et al.* 2000; Van Meijel *et al.* 2002d). This occurs in four successive phases:

1. The preparatory phase: In this phase, information is offered to the patient and the participating members of the social network. The object is to arrive at a joint basis for working with a relapse prevention plan. The nurse makes a systematic assessment of factors that can promote or hinder working with a relapse prevention plan and tries to influence these factors favourably (for example, with additional psycho-education if a lack of knowledge about schizophrenia and psychoses is apparent).
2. The listing of early warning signs: In this phase, the early signs are systematically inventoried. This inventorying is done as much as possible within the triad of patient - members of the social network - caregiver(s). The early signs are then worked out in operational terms in three levels of severity.
3. The monitoring phase: In this phase, the patient and the others involved receive instructions and assistance in the recognition and scoring of the early signs listed.
4. The preparation of an action plan: actions are formulated that can be performed by the parties when a psychotic relapse threatens. These actions are related to stress management, enhancing coping, and the application of protection from the surroundings. In addition, agreements are made about 24-hour availability of care.

The intervention protocol provides the nurse with a clear structure but also provides a great deal of room for adapting the methodology to the individual situation of the patient and the members of the social network.

Methods

Design

A randomised controlled trial with a follow-up period of 1 year was selected as the research design. Figure 1 presents the research design.

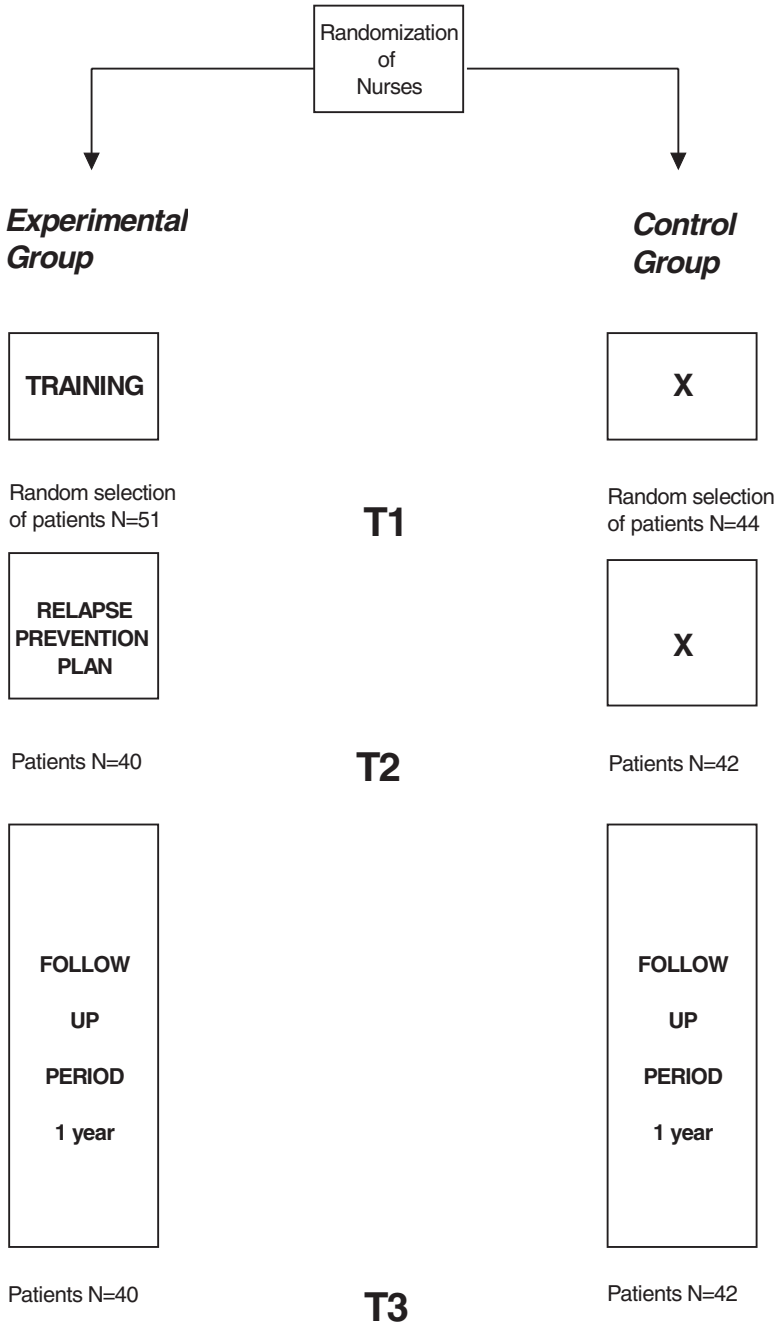

Figure 1

Subjects

Patients were included if they met the diagnostic criteria of schizophrenia or a related psychotic disorder according to the Diagnostic and Statistical Manual of Mental Disorders (APA 1994). The patient had to be stabilized to the extent that he or she could collaborate in the preparation of the relapse prevention plan. In

operational terms, this means that none of the items of the Positive Scale of the PANSS
(Positive and Negative Syndrome Scale / Kay *et al.* 1986) was higher than 4.

The patients could be hospitalised, be attending the day clinic, or be treated as outpatients. For the last treatment form, there had to be a minimum contact frequency of once every two weeks in the phase of the preparation of the relapse prevention plan. Finally, the patient had to be able to give informed consent to participate in the study.

Patients were excluded if there was organic brain disorder or mental retardation. Further exclusion criteria were serious alcohol and/or drug abuse insofar as this abuse was accompanied by serious communication and/or behavioural problems. The expectation was that these problems would seriously hinder constructive collaboration in working with the relapse prevention plan.

Patients who had participated the previous year in the Liberman module "Symptom Management" were also excluded. The content of this module is similar to the content of the intervention protocol. Patients who had previously been involved with other forms of early recognition and early intervention were also excluded.

The patients came from three mental health organizations: an institution for outpatient care and two mental health organizations with clinical, day-clinic, and outpatient care.

The randomisation of the nurses and patients proceeded as follows:
The administrators of the various departments compiled a list of nurses who would come into consideration for participation in the study. The selection criterion was that the nurse was capable of exercising the responsibility for the total nursing care of the patient and his or her social network. The selected nurses where then divided at random per department between the experimental and the control conditions. By randomisation at the department level, specific characteristics of the department and the treatment could be divided equally over both research conditions.
Next, the nurses then listed the patients under their care who met the selection criteria. The researcher determined at random the order in which the patients would be approached for participation in the study. This was done to avoid a selection bias. Ultimately, 1 to 3 patients were selected for each nurse to participate.

Procedure and data collection

The nurses who had been assigned to the experimental group were trained in the application of the intervention protocol in two training sessions. During these sessions, the underlying theory was explained, and role-playing exercises were used to practice the intervention. For the nurses in the control group, an information session was held in which they were informed in broad outlines about the research objectives and procedures.

The data collection then took place at three times (See Figure 1):
T1: After completion of the training sessions. This is when the patients were included.
T2: After the completion of the relapse prevention plans or a corresponding period in the control condition. This also marked the commencement of the follow-up period.
T3: After completion of the follow-up period of one year.

Table 1 gives an overview of the measurements at the various times.

For both conditions, the recruitment and selection procedure of the patients commenced after the completion of the training and information trajectory. The patients selected were first asked by the supervising nurses to participate in the study. If the patient agreed, he or she was visited by the researcher or a research assistant who provided him or her with further information about the study and the informed-consent procedure. After definitive agreement, the T1 measurements followed.

The nurses of the experimental group then prepared the individualized relapse prevention plans with the patients and, if possible, with members of the patient's network. The researcher here played a consultative and advisory role. The control group received care-as-usual. After completion of the relapse prevention plans in the experimental group, and after a comparable period of care-as-usual in the control group, the T2 measurements were recorded. Then commenced the follow-up period in which the relapse prevention plan was actually applied in the experimental condition. The nurses and the patients were instructed to score the early signs of the plan each week. The researcher provided separate scoring forms for this purpose. They had to act according to the actions in the relapse prevention plan when these early signs increased.

Table 1 : Overview of measurements				
		T 1	T 2	T 3
Variable	Instrument (filled in by....)			
Nurse				
Demographic data	Registration form (N)	X		
Training + work experience	Registration form (N)	X		
Patient				
Demographic data	CASH (R)	X		
Illness history	CASH (R)	X		
Psychopathology	PANSS (R)	X		
Psychiatric diagnosis	DSM-IV (D)	X		
Medication	Patient dossier (N)	X	X	X
Insight into psychosis	Insight Scale SR (P)	X	X	X
Insight into psychosis	Insight-Scale I (N)	X	X	X
Psychotic relapse	PANSS - PS (R)		total follow up	
Treatment setting	Registration form (N)	X	total follow up	
Patient – nurse				
Working alliance	WAI (P)	X	X	X

N = Nurse; P = Patient; D = Doctor; R = Researcher

During the follow-up year, the researcher had a consultative role for the nurses who performed the experimental intervention. Within the control condition, care-as-usual was continued. At the end of the follow-up year, the T3 measurements were taken.

Registration of relapses

Psychotic relapses and re-admissions were measured during the entire follow-up year. During this year, the nurses of both research groups were asked to telephone the researcher when a psychotic relapse occurred. At the beginning of the follow-up year, they received oral and written information on the evaluation criteria. To prevent under-relapse prevention of relapses, a progress-report form was given to all the nurses each quarter for each patient. This form was used to check the current data: the setting in which the patient was receiving care, the name of the nurse responsible for him or her, and whether or not a psychosis had occurred during the quarter. Each quarter, the relapse evaluation criteria were again brought in writing to the attention of the nurse. The frequency with which the early signs were scored was also registered each quarter in the experimental condition. In this way, we could determine the extent to which the relapse prevention plan was actually used in the treatment. If the progress-report forms were not returned, the researcher telephoned the nurse to ask for the required information. In this way, a reliable description of the condition of all of the patients could be established every three months.

An evaluation of a psychotic relapse was made in consultation between the nurse and the psychiatrist. In the first instance, one proceeded from the clinical evaluation: one can speak of a psychotic relapse when there is a significant increase of the following psychotic symptoms: (1) delusions, (2) hallucinations, (3) disorganization of thinking, which may be in combination with (4) chaotic and/or aggressive behaviour. In addition to this clinical judgment, the CGI (Clinical Global Impression) was also scored (Guy 1976). As criterion for relapse, we took a score of 6 or higher on the Global Impression Scale, which means that a severe to very severe deterioration of the general condition of the patient had occurred due to the psychotic symptoms ('much worse' / 'very much worse'). Further, the psychotic symptoms had to be present for at least 7 days to be considered a relapse.

The written report of the psychotic relapse on the progress-report form also indicated whether the patient had received a higher dose of antipsychotic medication and whether he or she had been admitted to hospital.

When the report was received, an independent researcher, who did not know the research condition of the patient, interviewed by telephone the nurse or caregiver who had been able to observe the patient during the psychotic episode. The interview was structured on the basis of the items of the Positive

Scale of the PANSS. This score was compared with the PANSS score on T1 in order to assess the relative increase of the psychotic symptoms.

Instruments

For research into the psychopathological characteristics of the patient, the Positive and Negative Syndrome Scale (PANSS) was used in this study. This scale was developed for the typological and dimensional evaluation of schizophrenic symptoms (Kay *et al.* 1987). The scale was tested extensively for validity and reliability with satisfactory results (Kay *et al.* 1986). Both the main researcher and the research assistant received PANSS training.

The insight into the illness of the patient was measured with the Insight Scale (Birchwood *et al.* 1994). This self-report scale consists of 8 items that cover the three dimensions of insight: (1) attribution of symptoms (2 items), (2) awareness of illness (2 items) en (3) need for treatment (4 items). The psychometric aspects of this scale are satisfactory. The scale was first translated into Dutch by Van der Gaag *et al.* (1994), and another translation was made by van Meijel *et al.* (2000), the objective being to obtain a univocal interpretation of the items. Van Meijel *et al.* (2000) also developed an informant version of the scale in order to obtain simultaneous evaluations of the insight by the patient and by the nurse.

The quality of the therapeutic alliance was measured with the Working Alliance Inventory (WAI) (Horvath & Greenberg 1989). This scale was translated into Dutch by Vervaecke & Vertommen (1993). It distinguishes three dimensions based on Bordin (1976): (1) the goal dimension: the agreement between the patient and the caregivers about the goals being worked for (12 items); (2) the task dimension: the agreement between the patient and the caregivers about the way in which the objectives can be achieved (12 items); (3) the bond dimension: the development of a personal bond between the patient and the caregiver (12 items). Little psychometric research has been done that has provided indications of sufficient validity and reliability of the scale. The high correlations between the subscales, however, cast doubt on the distinguishing capacity of the dimensions given. For our study, we used the client version of the scale. The items were reformulated to enhance the applicability to the nurse-patient relationship.

The Clinical Global Impression (CGI) (Guy 1976) consists of two simple subscales that measure the Severity of Illness and the Global Impression,

respectively. The Global Impression Scale refers to changes over the course of time and is thus of importance for our study. The scale is structured symmetrically: from Score 1 ('very much improved') via Score 4 ('no change') to Score 7 ('very much worse'). The Severity of Illness Scale was not used because it gives a more static evaluation of the severity of the illness at a given moment, which would be of less use for our study.

The Comprehensive Assessment of Symptoms and History (CASH) (Andreasen *et al.* 1992) is a comprehensive diagnostic instrument that compiles data on a large number of illness-related subjects. For our study, we used Sections 1 (socio-demographic data) and 4 (illness history).

For the antipsychotic medication, dosage equivalents were calculated with respect to haloperidol (Ziekenfondsraad 1999). The use of sedatives was scored dichotomously.

Data analysis

For the comparisons of the experimental and the control group, we used the Chi-square test, the Mann-Whitney U test and the T-test for independent groups in accordance with the measurement level and the group sizes. To estimate the treatment effect, a number of risk measures were also used.

To compare the "survival duration" of the patients in the two groups, that is, the period that they are free of psychosis, a survival analysis was performed (Kaplan Meier / Log rank test / Cox proportional hazard regression). Longitudinal changes in medication use, illness insight, and the quality of the therapeutic alliance as well as comparison of changes between the two groups were studied by means of Repeated Measures ANOVA and multi-level analysis. The latter analytical method makes it possible to take account of the variability on the levels to be distinguished: (1) the time of the data collection, (2) the level of the patient, and (3) the level of the nurse. The fixed effects, time, intervention group, and their interaction were here tested with a Likelihood Ratio Chi-Square Test. For those dependent variables where statistically significant effects were found, model estimates of the average scores are given for each of the times for each of the two groups.

Results

The nurses

The basic data were collected from the caregivers who had completed at least the period T1-T2. The total number was 48 of which 26 participated in the experimental group and 22 in the control group. Most of them had a nursing background (n=45). The rest (n=3) had been trained as social workers. The groups did not differ as regards the variables of age, sex, education, duration of employment, and years of experience.

Dropouts

At T1, a total of 95 patients were included: 51 in the experimental group and 44 in the control group. In the T1-T2 period, 11 patients dropped out from the experimental group and 2 from the control group. The reasons for dropping out are summarized here:

Experimental group (n=11)

- Premature discharge of the patient (n=1)
- The stress caused by preparing the relapse prevention plan (n=2)
- Psychotic decompensation (n=1)
- Lack of motivation to prepare the relapse prevention plan (n=5)
- Lack of time of the nurses (n=2)

Control group (n=2)

- Completion of the treatment (n=2).

We tested whether there were differences between the dropouts and the remaining patients on all T1 variables. The dropouts scored significantly lower on the Global Assessment of Functioning Scale of the DSM-IV diagnoses ($U=143$; $p<.05$), which indicates a lower general level of functioning. Further, their PANSS scores were significantly higher ($U=254$; $p<.05$). The higher PANSS-scores were due to the higher scores on the General Psychopathology Subscale ($U=261.5$; $p<.05$) and the Negative Subscale ($U=329$; $p<.05$), but not on the Positive Subscale ($U=452$; ns). This means that the dropouts did not have different psychosis-related symptoms than the remainers.

Baseline measurements

Table 2 gives an overview of the baseline measurements at T1 of the remaining patients who started and completed the follow-up period. The patients who dropped out between T1 and T2 are excluded in this baseline comparison. No significant differences were found for any of the variables at this time between the experimental and the control group, with the exception of the variable of sex: The experimental group has relatively more women than men ($X^2_{(1)} = 4.082$; $p<.05$). This means that, although dropouts differed from the remainers, experimental and control group patients were comparable at baseline.

Relapses

In the experimental group, 40 relapse prevention plans were prepared. The average number of days devoted to this was 155 (SD=94). The corresponding period of non-intervention in the control group was on average 145 days (SD=70), this difference not being significant ($t_{(80)} = -.549$; ns).

The frequency of scoring of the early signs in the experimental group indicated a slight decline in the course of the follow-up year, but the average was between 5 and 9 scores per quarter for the entire year. Six patients did not score any longer by the end of the follow-up year: three for lack of motivation, one because of a long-term psychosis, one because of detention, and the sixth because things were going very well with her and so she did not see the need for regular scoring.

Table 3 gives an overview of the relapse rates in the two groups.

Table 2: Baseline Comparisons				
Variable	*Experimental group (n=40)*	*Control group (n=42)*	*Test*	*P*
Age, mean	35.2	34.5	$t_{(80)} = - .345$	p =.73
Male sex	28 (70%)	37 (88%)	$X^2_{(1)} = 4.082$	p =.04*
Marital status / single	33 (83%)	32 (76%)	$X^2_{(1)} = .496$	p =.48
Dutch nationality	37 (93%)	39 (93%)	$X^2_{(1)} = .004$	p =.95
Educational level Primary school / lower vocational school Other education	 15 (38%) 25 (62%)	 24(57%) 18 (43%)	$X^2_{(1)} = 3.170$	p =.08
Paid employment	5 (13%)	12 (29%)	$X^2_{(1)} = 3.220$	p = .07
Organized activities	16 (40%)	15 (36%)	$X^2_{(1)} = .160$	p = .69
DSM - 1 schizophrenia schizo-affective disorder other psychotic disorders	 24 (60%) 11 (28%) 5 (12%)	 33 (79%) 6 (14%) 3 (7%)	$X^2_{(2)} = 3.345$	p = .19
DSM - 5 / mean	56.3	58.8	$t_{(80)} = 1.032$	p = .31
Care intensity Ambulatory care Semimural care Clinical care	 28 (70%) 5 (12.5%) 7 (17.5%)	 33 (79%) 2 (5%) 7 (16%)	$X^2_{(2)} = 1.648$	p = .44
Age at onset / mean	23.1	23.5	$t_{(80)} = .315$	p = .75
Sickness duration in years / mean	12.2	11.0	$t_{(80)} = -.589$	p = .55
Number of psychoses / mean	4.4	3.8	$t_{(80)} = -.612$	p = .54
Medication / haloperidol equivalents / mean	5.1	5.5	$t_{(80)} = .505$	p = .62
Sedatives	13 (33%)	19 (45%)	$X^2_{(1)} = 1.199$	p = .28
PANSS total / mean PANSS Positive Scale / mean PANSS Negative Scale / mean PANSS- General Psychopathology / mean	63.9 13.7 15.6 34.1	60.4 12.2 15.9 31.6	$t_{(70)} = -1.037$ $t_{(79)} = -1.599$ $t_{(77)} = 0.254$ $t_{(73)} = -1.528$	p = .30 p = .11 p = .80 p =.13
Insight Scale - SR / mean Insight Scale - I / mean	10.4 10.3	9.66 10.7	$t_{(72)} = -1.182$ $t_{(74)} = .805$	p = .24 p = .42
WAI / mean	134.1	133.8	$t_{(73)} = -.085$	p = .93

Table 3: Relapse outcomes				
		Experimental group	Control group	Total
Relapse	NO	35 (87.5%)	31 (73.8%)	66
	YES	5 (12.5%)	11 (26.2%)	16
Total		40 (100%)	42 (100%)	82

The relapse rates in the experimental and the control groups were, respectively, 12.5 and 26.2%. Testing showed that this difference is not significant ($X^2_{(1)} = 2.445$; $p = .12$). In addition to the conventional testing with the Chi-square test, a number of other measures were calculated that give an indication of the treatment effect.

The *Relative Risk (RR)* of a relapse in the intervention group with respect to the risk in the control group is 0.48 (CI 95%: $0.20<X<1.26$). The *Relative Risk Reduction (RRR)* is 0.52 (CI 95%: $-0.26<X<0.80$), which means that the chance of a relapse declines by 52% by application of the intervention. The *Absolute Risk Reduction (ARR)* is 0.137 (CI 95%: $-0.031<X<0.305$), which implies that a relapse can be prevented with the intervention protocol in almost 14 patients out of a 100.

The *Number Needed to Treat (NNT)* is 7.3 (CI 95%: $3.28<X<\infty$). This means that the intervention must be applied to a good 7 patients to prevent a psychotic relapse in one of them.

The interpretation of the Relative Risk is simpler when this risk is expressed as a number greater than 1 ($1/RR = 2.095$ / CI 95%: $0.79<X<5.00$). The conclusion is then that the risk of relapse found is twice as great in the control group as in the intervention group. A 95% confidence interval for this relative risk runs from 0.79 to 5.00, which indicates that the effect found is not statistically significant (see Figure 2).

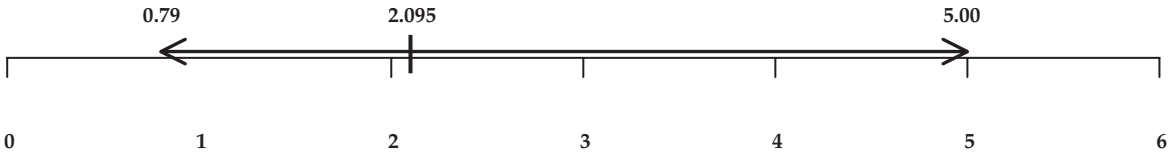

Figure 2: Relative Risk of psychotic relapse + confidence interval (control group versus experimental group).

Figure 3 gives the Kaplan-Meier survival curves for the experimental and the control group for the follow-up period of one year. The mean survival time of the experimental group was 329 days, for the control group 296 days. The Log Rank Test revealed no significant differences ($\text{Log Rank}_{(1)} = 2.28$; $p=.13$)

The scores on the PANSS / Positive Scale increased for the decompensating patients in the control condition from 14.1 (baseline measurement) to 26.4 (time of psychotic relapse) (Wilcoxon Signed Ranks Test $z=2.371$; $p<.05$) and for the decompensating patients in the experimental condition from 17.2 to 30.2 (Wilcoxon Signed Ranks Test $z=2.023$; $p<.05$). This increase is significant in both groups.

With two exceptions – one patient in the control group and one patient in the experimental group – all of the patients who had a relapse were prescribed a higher dosage of medication. All of the patients from the experimental group were admitted to the clinic because of the relapse. In the control group, two of the patients received intensive home care to cope with the crisis; six were admitted to an intensive clinical care unit, and three others were already receiving clinical care at the time of the relapse.

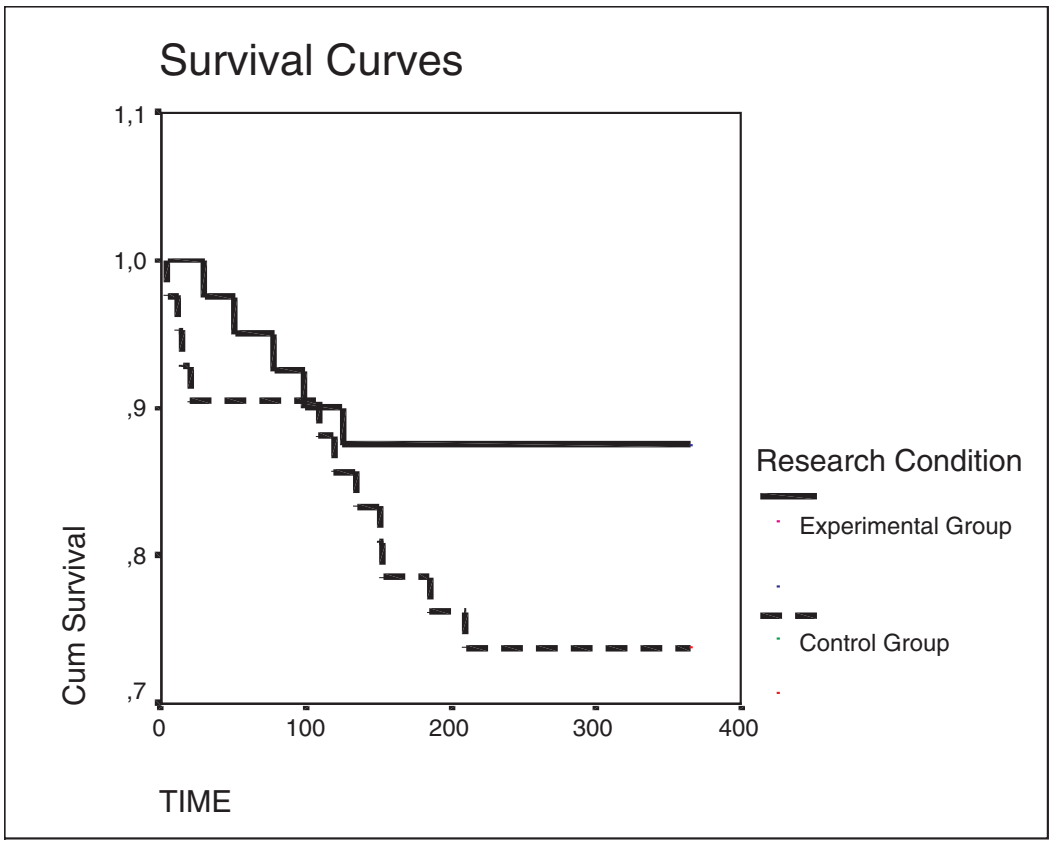

Figure 3: Kaplan-Meier Survival Curves.

Other variables

With regard to the consumption of medication of the patients, no significant time and/or intervention effects were found (p>.10). Thus, application of the intervention did not lead to significant changes in medication consumption.

This applies also for the total scores on the Insight-Scale IS, both for the self-report version and for the informant version. In the three subscales of the IS, a significant effect is found on the subscale 'attribution of symptoms' of the self-report version (p=.04). The measurements on the Working Alliance Inventory give significant time-intervention interaction effects on the total score (p=.03), on the goal dimension (p=.05), and on the bond dimension (p=.02).

Examining the average scores of these variables, we see that the significant effects can be explained primarily by the relatively irregular score pattern

within the control group, and this with relatively stable scores within the experimental group (see Table 4).

Table 4 : Secondary Outcome Measures			
	T1	**T2**	**T3**
Variable			
Working Alliance Inventory			
WAI – total score			
• experimental group	134.1	135.6	135.1
• control group	133.2	129.2	138.2
WAI – goal dimension			
• experimental group	39.8	40.1	38.5
• control group	39.1	38.1	40.9
WAI – bond dimension			
• experimental group	47.3	47.7	47.6
• control group	47.5	45.5	48.8
IS-SR 'attribution of symptoms'			
• experimental group	3.4	3.5	3.7
• control group	3.4	3.7	3.3

Table 4: variables with significant time*intervention interaction effects ($p<.05$)

Discussion

The study presented here gives the effects of a nursing intervention with the objective to prevent psychoses in patients with schizophrenia or a related disorders. The intervention was developed on the basis of (1) a study of the literature and (2) qualitative research into already existing practices of comparable interventions. An element of this developmental trajectory was that experts in the area of the care of schizophrenia evaluated the intervention.

The intervention was then tested in a number of case studies. The components of this developmental trajectory yielded the qualitative evidence needed for the effectiveness and practicability of the intervention.

The randomised controlled trial described here involved stabilized patients who met the diagnostic criteria of schizophrenia or a related disorder within the schizophrenic spectrum. The dropout in the experimental group puts into question the comparability of the experimental and control group. With a dropout rate of 22% the effects of randomisation on achieving comparability between experimental and control condition is put in jeopardy. It should, however, be noted that the comparison of experimental and control groups excluding the patients who dropped out, show that those who remained in both groups are comparable at T1. Not only are the differences not significant, but those who remained in the experimental group have less favourable (but not significantly different) means than the remainders in the control group on those variables in which dropout and the remaining patients differ. When comparing the baseline measurements with all the patients who were included the patients in the experimental group had a significantly lower level of general functioning that the patients in de control group ($t_{(86)}$=2.028; p= .046). Therefore the likelihood that differences in the groups are a probable alternative explanation of the findings is low. Apparently, the randomisation did not result in comparable groups at the moment of inclusion, and correction might have been needed if all patients remained in the study. The relatively high dropout rate in the experimental group during the execution of the intervention (before the start of the follow-up year) shows that the efforts involved in preparing a relapse prevention plan cannot be sustained by all of the patients or the nurses. The patients who dropped out had a significantly lower level of general functioning and more psychopathological symptoms.
Women were significantly over-represented in the experimental condition during follow-up. This could have slightly distorted the results because the disease process in women is, in general, slightly more favourable than in men.

The reliable measurement of psychotic relapse is not without problems. Linszen (1993) shows in a review of the literature how different the definitions and measurements of psychotic relapse are. Sometimes, clinical readmission suffices as the criterion. However, this is not an adequate criterion because schizophrenic patients can be admitted for a very wide range of reasons. In other studies, the clinical judgment is used as the criterion: there is a relapse

when the caregivers call it one. A scientifically more justified measurement is obtained when testing is done with a certain regularity on the basis of relapse criteria prepared in advance, with the aid of validated measurement instruments such as the PANSS. In our study, we sought a compromise that was compatible with the logistical efforts that could be carried out at the three locations where the research was conducted. This compromise consisted of complementing the clinical judgment of the caregivers by the score on the CGI, the 7-day criterion, and the interview with the caregivers by a research assistant who was blind for the research condition of the patient. This was combined with a three-monthly contact with the nurse in which all the information regarding the course of the illness was again checked. The significant increase of psychotic symptoms in relapsed patients confirms that, with the criteria selected, we were indeed able to track the most serious relapses. A potential problem seems rather to be in the cases where the caregivers decided that the criteria were not met by a small margin and so decided not to report the change in the status of the patient. Periodic measurements with established relapse criteria could resolve this problem but this would require, as noted, a much greater research capacity.

In view of the relapse outcomes in both groups, we can state that a difference is indeed apparent in the desired direction, but that this difference is not significant with conventional testing (X^2) (p=.12). Survival analysis shows a comparable p-value.

It must be noted that the relapse rate in the experimental group is very low (12.5%). This percentage is also found in studies with optimal treatment conditions. Even the relapse percentage in the control group may be considered low for regular treatment conditions. As already indicated in the introduction, this percentage is generally estimated at about 35 - 40% (Kissling 1991 / 1992; Ayuso-Gutierrez & Del Rio Vega 1997; Tarrier 1997; Wirshing *et al.* 1991; Liberman & Kopelowicz 1995; Viguera *et al.* 1997). A contamination effect between the experimental and the control group cannot be excluded. Randomisation on the unit level inadvertently has the result that experimental-group nurses communicate with control-group nurses about the research and the intervention, which could have positive effects on the working methods of the latter.

In both groups, aspecific effects could have occurred alongside the therapy-related effects such as the Hawthorne effect: the extra attention that nurses and patients receive because of their participation in the study could generate treatment effects independent of the specific intervention.

The sample size must also be discussed here. In the design of the study, relapse rates of 15% (experimental group) and 40% (control group) were assumed when the sample size was determined. A size of 48 people per group would then suffice (α=.05; β=.80). Although the inclusion of patients remained somewhat lower than expected, the failure of the relapse rate in the control group to exceed 26% was one of the reasons why the proportional differences did not reach statistical significance. A considerably larger sample is needed for significance given these relapse rates.

Conventional testing with p-values alone is insufficient for adequate estimation of the treatment effect (see also De Haan *et al.* 1998). Therefore, a number of risk measures were calculated as well. The RR of 2.095 indicates that in this study a positive effect of the intervention was found, but the effect observed is not statistically significant. Here too, the sample size may cause the difference not to be significant.

The Number Needed to Treat is interesting from the perspective of cost effectiveness. The question is with how many patients does the intervention need to be executed in order to achieve the intended result in one of them. In our study, this is a good 7. More extensive cost-effectiveness research is required to quantify the additional effort of caregivers needed to prepare a relapse prevention plan and to work with it in order then to relate it to the average costs that are saved by the prevention of a psychotic relapse.

In our opinion, it is important to see the intervention studied here as part of a more comprehensive treatment program of which other components also contribute to reducing psychotic recidivism. Included, of course, are pharmacological therapy and also various forms of skill training, supportive family therapy, and cognitive therapy. It is precisely the combined application of these intervention possibilities that will achieve the most favourable treatment results.

The expectation was that the intervention would generate increased insight into the illness, that the work alliance would change between the patient and the nurse (in particular in the task and goal dimensions), and that lower doses of medication would be prescribed because of the reduction of psychotic relapse. The multilevel analysis led to the conclusion that there were significant differences regarding the work alliance (total score, bond and goal dimension) and the insight/attribution of symptoms. However, the interpretation of these results is difficult because they are influenced primarily by a relatively irregular score pattern at the various time points in the control condition.

The possibilities of comparing our research results with results of other studies are few. Methods of early recognition and early intervention have indeed been used in various studies, but then mostly in combination with divergent medication strategies whereby the effect of early intervention cannot of itself be determined.

An exception to this is the study of Herz *et al*. (2000). They standardized the medication administration and examined the effects of a Program for Relapse Prevention. They compared this intervention program with a control condition in which care-as-usual was offered. Active monitoring of early signs was combined with psycho-education and weekly group therapy for patients and family meetings (multi-family groups). After 18 months, they found significant differences between the two groups as regards psychotic relapses and rehospitalisations.

The study of the effects of the Liberman Modules certainly deserves mention here. This consists of a modular treatment supply in group therapy oriented to various skill areas. The "Symptom Management" module is directed to early recognition of psychotic relapse. It is certain that these modules have a positive effect on the acquisition of new knowledge and skills (Wallace & Liberman 1995; Wallace *et al.* 1992; Eckman *et al.* 1992; Goulet *et al.* 1993). The effect on rehospitalisations was studied by Stenberg *et al. (*1998), who concluded that the training had no significant effect on the number of readmissions but did have one on their duration.

It is important that effectiveness research in this area be continued in which the psychotic relapse is used as the primary result. The intensification of research within nursing practice is, in our judgment, of great importance because a considerable portion of the therapeutic efforts is and can be executed with the context of nursing care.

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Chapter 9

General discussion

Introduction

This thesis describes the development and testing of a nursing intervention protocol and examines its effects when applied in nursing practice, with the aim of helping to prevent psychotic relapses in patients with schizophrenia or a related psychotic disorder. The gradual process leading up to a psychotic episode offers possibilities for preventive intervention. If action is taken at an early stage of the relapse process, a psychotic crisis can be avoided.

The literature overview in Chapter 2 clearly shows that research in the areas of early recognition and early intervention is still in the initial stages. On the basis of the literature described, we may conclude that the majority of psychoses are preceded by early signs and that these early signs are also recognised by the majority of patients and their family members. Furthermore, the studies offer an insight into the nature of the early signs, as well as the relative frequency with which they appear. When the studies were discussed in terms of the predictive value of the early signs, we concluded that the sensitivity values in the different studies varied largely (8-81%). A closer examination of the studies led us to assume that the predictive value of the early signs can be perfected if an individual profile of these signs (including pre-psychotic and idiosyncratic symptoms) is drawn up for each patient. This will, pragmatically, dispense with the need to engage in a theoretical discussion about where the borderline lies between early signs and (pre) psychotic symptoms. We argued that this differentiation is of less importance in clinical practice. The primary aim is early detection, whereby the maxims "the earlier the better" as well as "better late than never" apply.

Noticeably, little work has been done in terms of the development of intervention programmes for early recognition and early intervention. Although the principles of early recognition and early intervention have been applied frequently in medication studies, the methods used have hardly ever been worked out in any greater detail. Liberman and his colleagues are the exception in that they designed a group education program for the target group of chronic psychiatric patients aimed at "symptom management" (Wirshing *et al.* 1991; Eckman *et al.* 1992). Herz *et al.* (2000) also described an intervention program aimed at early recognition and early intervention. The results of experimental studies into the effects of these programmes, limited in number as

they may be, are positive in that the programmes have led to the patient acquiring a greater knowledge of symptom management and skills necessary to achieve this, and to less psychotic relapses and re-admissions to psychiatric institutions (Wirshing *et al.* 1991; Eckman *et al.* 1992; Herz *et al.* 2000; Stenberg *et al.* 1998). More intervention studies are required in order to further substantiate these first promising results.

The starting point of our study was that we wanted to develop a nursing intervention protocol for early recognition and early intervention suitable for application in the one-to-one situation between patient and nurse. Nursing staff play a central role in the care of schizophrenic patients. Therefore, they are in a position to monitor the condition of the patient in a structured and effective manner. There is an enormous need within the nursing profession for methods that would support their working practices.

Intervention development

The search for literature on intervention development methods in a nursing context produced exceptionally few results (see Chapter 3). Apparently, the development of nursing interventions is a neglected issue in EBP. This is remarkable, given the complex nature of the intervention development process. The intervention development model presented in Chapter 3 tries to shed light on some aspects of the methods used in this process and to provide a structure on the basis of which intervention development can be given shape. The model offers a number of time options which are important to ensure that the development and testing of the intervention are carried out both efficiently and to a high standard of quality. Criticism can be levelled at the one-sided manner in which those supporting evidence-based practice place emphasis on the quantitative testing of the effectiveness of interventions. Our argument is that such testing cannot take place until attention has been given to a careful intervention development procedure. Otherwise, the risk of testing a (theoretically) poorly set up intervention would be too great. This certainly applies in the case of interventions common in (psychiatric) nursing that are complex and are made up of several elements.

The efforts put into the quantitative testing of the effects may become less expedient once intensive investment has gone into the development of the intervention. To determine the effects of our intervention, we opted for a randomised controlled trial. The effectiveness of our intervention was to be measured by a drop in the number of psychotic relapses. Such a result can be determined only through an experiment, followed by a follow-up period of a minimum of one year.

A method for early recognition and early intervention

The intervention that is the subject of this study is a complex intervention. It is complex because, based on the literature data available to us, we realised that the intervention should be comprised of different elements and stages which could not be filled in with any concrete precision a priori. It is also complex in that the intervention should be performed within a social system in which the mental health nurse, the patient, the patient's family and other members of the social network have a role. An intervention becomes more complex the more players are involved. However, the intervention is particularly complex because of the variability within the target group: it was obvious beforehand that the nurse's intervention strategy could differ from one patient to the next. In cases where there are numerous time options that can influence the effectiveness of the intervention with respect to an individual patient, there is all the more reason to substantiate these options well. In order to formulate the intervention program, it was necessary to gain an understanding of the desired intervention structure as well as the factors, which could have a positive effect on the performance of the intervention. Already existing intervention practices were studied for this purpose.

Current practice analysis

The study of existing intervention methods offered us the opportunity to gain insight into the already existing working procedures in nursing practice. It also gave us the opportunity to learn from the experiences of nurses, patients and family members. The qualitative interview and analysis techniques were of great value in interpreting the intervention practices and in gaining an understanding of the critical success factors when applying the

early recognition and early intervention methods. The results are described in Chapters 4 and 5. In retrospect, we would say that it would have been a missed opportunity had we not used the data from these practices. The methodical procedures, the experiences of those involved and the critical factors in performing the intervention were lucid and were valuable in the stage of intervention design. A critical comment on the non-randomised selection of respondents is in order. They do not reflect the average health care practice, but are rather the vanguards of the practice. However, for the purposes of our research, this was rather beneficial than it was a problem. Given their expertise, the health care workers were able to consider a larger number of cases, in which working with relapse prevention plans turned out well in some instances but badly in others. On the one hand, this provided the information necessary to describe an ideal practice, whilst on the other it enabled the recognition of factors which prevented such an ideal situation being created.

In this exploratory phase of the research, particular attention was paid to the patient's subjective experiences and his need for care. The successful performance of a program for early recognition and early intervention depends largely on the extent to which it accommodates the patient's personal experiences and care needs. The patient's motivation and involvement are essential variables in the process and strongly influence the effectiveness of the intervention. When implementing the newly developed intervention on a wider scale, due regard must be had to the fact that practices may be much more intransigent than the ones we came across in these vanguard practices.

Intervention Design

The qualitative research phase shed light on the fact that a compromise should be reached between (1) introducing sufficient structure into the intervention protocol so as to give the nurse and the patient enough to go on when performing the intervention and (2) creating sufficient scope so that the execution of the intervention can be adapted to the patient's personal characteristics and the context of the care provided. In our opinion, there should also be room for the individual nurse's personal manner of work, to the extent that this does not contravene existing scientific evidence. To assume that nursing staff would be prepared to alter their working methods from one minute to the next as a result of rules in an intervention protocol

would, in our view, be naive. Motivation is just as important for the nursing staff who are to carry out the intervention as it is for the patient target group. Therefore, stipulating to the nursing staff the exact procedures to follow would be inconsistent with this principle. Nor would it be desirable, as we shall now demonstrate.

The ability to deviate from guidelines and protocols with a view to providing care tailored to the individual is, in our opinion, an important characteristic of professionalism. This leads to care becoming individual in nature, i.e. tailored to the ability, wishes and needs of the individual patient. Some authors (including Liberman *et al*), who are advocates of a more standardised intervention approach, do not sufficiently recognise the need for an individualised intervention strategy. They argue that an intervention must be carried out to the letter if it is to have any effect. However, this has not been proven scientifically and is not defensible from an epistemological point of view.

Perhaps such standard procedures would be desirable in a homogenous population of patients having similar problems, which they perceive in a similar way and for which a more or less clear-cut solution can be found. This is by no means the case with schizophrenia and its related problems. There are so many variants of the disorder, its manifestations and the consequences for the patient and others involved, that a uniform intervention strategy can be all but ideally effective. The variability between patients is so great that Vlaminck (2002) concluded that patients suffering from schizophrenia or a related disorder have very little in common with each other. Therefore, according to Vlaminck, developing standard intervention programmes does not do justice to reality. In addition to the various forms of schizophrenia as a psychiatric disorder, many other variables could be mentioned which require individualised intervention strategies. A disorganised schizophrenic patient who has had frequent psychotic relapses, who has serious cognitive limitations, who has no insight into the illness and is not motivated to obtain treatment, and who has no social support structure requires a totally different approach from a patient who has only experienced a paranoid psychosis once and who is prepared to take preventive measures to avoid future relapses.

It is not inconceivable that care is standardised to such an extent as to inflict iatrogenic harm, for example, by causing stress to the patient or undesirable confrontation with psychopathological terms in case there are

serious acceptance problems. On the other hand, care may also be standardised to such an extent as to lead to under-stimulation, in that insufficient use is made of the capabilities, which the patient possesses.

The intervention protocol, the content of which is described in Chapter 5, attempts to provide the nurses with a certain amount of structure during the execution of the intervention. At the same time it leaves them sufficient room to make their own decisions to adapt the treatment in such a way as to do justice to the individual features of the patient and his social network, the differences in perception, capabilities, wishes and needs, and the differences in the context within which care is offered. The opinion of experts in the field of schizophrenia care on the draft intervention protocol has led to adjustment of the protocol. The reservation they showed related, for the most part, to whether the protocol could actually be implemented. They wondered whether the detailed specifications within the protocol might be too much at the expense of its usefulness to the individual nurse and therefore, at the expense of the protocol's applicability in nursing practice. The case studies made of nine patients to test the feasibility of the intervention protocol in nursing practice confirmed the experts' opinion. A version of the protocol that was easier to use was required if its usefulness in nursing practice was to increase. A more concise version of the protocol was, therefore, developed before its effectiveness was tested on a larger scale in the randomised controlled trial.

The RCT

The main aim of the intervention protocol is to help prevent the occurrence of psychotic relapses in the target group concerned. As has already been stated, the only way to demonstrate the effects of such an intervention is to carry out an experimental study in which the psychotic relapses are registered and compared under experimental and control conditions during a certain follow-up period. The research into the effects, which was carried out as part of this thesis, did not provide any significant results. The conclusion – based partly on the Relative Risk – was that there are reasons to expect positive effects from the intervention. Not only was the rate of relapse in the experimental group unusually low (12.5%), the rate of relapse in the control group was also lower than the 40% which had been expected

based on scientific literature data. Our study showed a relapse rate in the control group of just over 26%. This result may, in part, have been caused by both contamination and the Hawthorne effect.
Another question to be asked, however, was whether our care-as-usual conditions matched the care-as-usual conditions in the relevant literature. Given the range in the nature and organisation of care for schizophrenic patients, nationally and internationally, relatively large differences in the rate of relapse are to be expected. Health care in the Netherlands scores relatively high points for the nature of its care, the way in which care is organised and the quality of its health insurance system compared to other countries, which would contribute to reducing the rate of psychotic relapses.

The question has to be asked whether the risk of finding insignificant results when setting up experimental studies such as this one, with a limited sample size, was not excessive. When making the power analysis for this study, we took as our starting point the proportional difference in psychotic relapses of 25%-30% between the experimental group and the control group.
If we assume more modest expectations, then the sample size will have to be increased in order to retain sufficient statistical power. For example, if we assume a rate of 15% for the experimental group and 30% for the control group, then a sample size of approximately 120 persons for each group would be required in order to achieve a statistical power of .80 (α=.05). A much larger sample would confront the researchers with yet another problem, namely the logistical efforts needed to carry out such an experiment. Enlisting the help of mental health care institutions, nursing staff and patients requires considerable effort in such a case, as well as the training of nursing staff, the implementation of the intervention, the completion of the follow-up program and the gathering of all the relevant data. Trebling the number of participants may be desirable, but at the same time, it is extremely costly. Moreover, there is a very great danger when striving for really large samples in field experiments that the researchers are unable to maintain sufficient control to ensure comparable conditions during the whole of the study and at all locations where the study takes place. This loss of control might very well outbalance the benefits of the large sample.

Certainly, when a reasonable case has already been made for the value of an intervention during the development stage and the first qualitative testing, the question of whether such large and costly trials should be set up is

highly debatable. It might be better to use the research funds available to provide answers to new research questions.

The problem inherent in carrying out a pragmatic trial is that it is not always sufficiently clear what actually happens under experimental and control conditions. One possible way of keeping track of what goes on is to carry out an intervention check. We did this in our study by carrying out a survey (see Chapter 8). Using a number of structured questions, we asked the nurses about their precise working procedures during the execution of the intervention. The survey, of course, was only an indirect intervention check. A direct observation of the working procedures would have been a more reliable gauge. However, in the context of our research, this was not feasible for practical reasons. The survey offered an insight into the nursing staff's procedures and it became clear that they followed the structure of the intervention protocol fairly precisely. The tendency to give socially desirable responses was discouraged by pointing out that deviation from the protocol, backed up by reasons, was legitimate and desired in cases where it contributed to achieving the set goal, i.e. the drawing up of a relapse prevention plan tailored to the personal situation of the patient. Criticism can also be levelled at the fact that few checks were carried out on the activities of the nurses in the control group. At the beginning of the study, they were instructed not to use any structured early intervention methods for the duration of the research. We do not know whether they actually observed these instructions. A number of nurses were certainly well acquainted with the early recognition and early intervention principles. A number of them were disappointed that they had not been selected to be part of the experimental group, in view of their motivation to draw up a relapse prevention plan together with their patients. It is almost inconceivable that the forced desistance from the use of any form of expertise was sustained.

By carrying out the survey, we were able to avoid a "black box" situation, where the effects of the intervention are measured without revealing the actual nature of the intervention. As already stated, practices were made less visible for the control group. Perhaps it would have been better to have asked the nursing staff about their actual working practices on a regular basis and, in particular, about their refraining from performing early recognition and early intervention.

Also important is the question who benefited from the intervention and who did not. Patients were included in the study who were psychiatrically diagnosed as suffering from schizophrenia, schizoaffective disorder and schizophreniform disorder. Another criterion for inclusion in the study was that the patients had to be sufficiently stabilised: the scores for individual items on the PANSS Positive Scale were not to exceed 4 points. The assumption was that if patients were not sufficiently stabilised, they would not co-operate sufficiently to draw up a relapse prevention plan. The patients who dropped out at the point when the relapse prevention plan was being drawn up functioned at a significantly lower level and had a higher level of psychopathological symptoms. This significant difference was found in the total PANSS-score and in the General Psychopathology and Negative Symptoms subscales, but not in the Positive Symptoms. The inclusion criterion of a maximum of 4 points on the PANSS Positive Score scale is probably the reason why no significant differences were found on the Positive Scale.

When the level of psychopathology is high, the chances of the intervention succeeding must be weighed even more carefully. The health care professionals who were interviewed during the exploratory study had already come to the same conclusion (see Chapters 4 and 5).

The sample size was too small to carry out sub-group analyses as part of the RCT. The results of the exploratory study offer a better tool to determine who benefits from the intervention and who does not. Based on their own experiences, the respondents who were interviewed indicated what factors contributed to the successful implementation of the early recognition and early intervention methods. A rule in our study was that the absence of suitable conditions for the successful performance of an intervention was not a reason *a priori* to put off the intervention for the patient concerned. Instead, it was considered the responsibility of the nurse to alter her working strategy so as to compensate for the unfavourable conditions or to improve these conditions through direct nursing activities. There were essentially two important reasons in our study - apart from failure to comply with the inclusion criteria - for not performing an intervention, namely (1) the patient's refusal and (2) the detection of adverse effects, for example, in the form of rising stress levels in a patient as a result of the intervention. One should not be too biased and base an intervention's chances of success only on the characteristics of the patient and the social context; they should also be

weighed based on the professional ability of the nurse to deal with these characteristics in a creative and hence flexible manner.

Taking stock

What are the conclusions to be drawn from the results of this thesis? If we look at mental health practices during the last few years, we notice that steps have been taken spontaneously to develop and apply early recognition and early intervention methods. In our opinion, this has happened because it involves a preventive intervention strategy, which is, in fact, sheer common sense. If one wants to prevent something from occurring (for example a psychosis), then one has to get on top of the problem as soon as possible and take preventive measures to avoid a more serious disaster. The study into existing intervention practices confirmed the value of such forms of intervention. It emphasised the need to standardise the existing methods more and to make them more usable in nursing practice. That was the exact aim of this study. The aim was not to devise something completely new but rather to standardise and structurise nursing procedures, using know-how available in the field of nursing and other relevant disciplines. In this respect, this study is hardly pretentious or even innovative. However, it touches on the essence of what has to be done in psychiatric nursing in the next few years, namely the application of available scientific knowledge which can be used by nursing staff and which dovetails with the patient's problems, needs and care demands.

The importance of the intervention was for the most part judged positively by nurses and patients in the case studies conducted and during the RCT. In fact, the importance of interventions should not only be judged in terms of their ability to prevent psychosis relapses and re-admission to an institution, but also in terms of their contribution to the self-management of the illness, to the patient's self-confidence to control the course of the illness and to the possibilities it offers to control responsibilities better in times of crisis (see Chapters 4 & 5). The study on the effects of early intervention somewhat throws a spanner in the works. However, that does not seem to be a reason to discontinue the project. Generally speaking, introducing an intervention on a wide scale should be conditioned on it being evidence-based, supported by significant effects on the primary result variables. In our

study, there seems to be reason to take the opposite position, namely to introduce the principle of early intervention on a wide scale until it is – unexpectedly - proven to be of little value.

References

Algra, A. & Graaf, Y. v. d. (1999). Dwalingen in de methodologie. Pragmatische en pathofysiologische trials. [Rooming through methodology. Pragmatic and explanatory trials: a matter of research question]. Nederlands Tijdschrift voor Geneeskunde, 143, 514-517.

Amador, X. F., Strauss, D. H., Yale, S. A., Flaum, M. M., Endicott, J., & Gorman, J. M. (1993). Assessment of Insight in Psychosis. American Journal of Psychiatry, 6, 873-879.

Andreasen, N. C., Flaum, M., & Arndt, S. (1992). The Comprehensive Assessment of Symptoms and History (CASH). An instrument for assessing diagnosis and psychopathology. Archives of General Psychiatry, 49, 615-623.

APA / American Psychiatric Association (1994). Diagnostic and Statistical Manual of Mental Disorders / DSM-IV. (4 ed.) Washington: APA.

APA (1997) Practice Guidelines for the Treatment of Patients with Schizophrenia. Am.J.Psychiatry, 154, 1-63.

APA (American Psychiatric Association) (2000). Diagnostic and Statistical Manual of Mental Disorders-IV-TR.

Ayuso-Gutierrez,J.L. & Rio Vega,J.M.d. (1997) Factors influencing relapse in the long-term course of schizophrenia. Schizophrenia Research, 28, 199-206.

Backer, T. E., Liberman, R. P., & Kuehnel, T. G. (1986). Dissemination and Adoption of Innovative Psychosocial Interventions. Journal of Consulting and Clinical Psychology 111-118.

Baker,C. (1995) The Development of the Self-Care Ability to Detect Early Signs of Relapse Among Individuals Who Have Schizophrenia. Archives of Psychiatric Nursing, 5, 261-268.

Baker, C. (1996). Subjective experience of symptoms in schizophrenia. Canadian Journal of Nursing Research, 28, 19-34.

Bellack, A. S. & Mueser, K. T. (1993). Psychosocial Treatment for Schizophrenia. Schizophrenia Bulletin, 19, 317-336.

Birchwood,M. (1992) Early Intervention in Schizophrenia: Theoretical Background and Clinical Strategies. Br.J.of Clin.Psychology, 31, 257-278.

Birchwood,M., Macmillan,F. & Smith,J. (1992) Early Intervention. In M.Birchwood et al. (Eds.), Innovations in the Psychological Management of Schizophrenia (pp. 115-145). Chichester: J. Wiley & Sons.

Birchwood,M., Smith,J., Macmillan,F., Hogg,B., Prasad,R., Harvey,C. & Bering,S. (1989) Predicting relapse in schizophrenia: the development and implementation of an early signs monitoring system using patients and families as observers, a preliminary investigation. Psychol.Med., 19, 649-656.

Birchwood,M. & Spencer, E. (2001) Early intervention in psychotic relapse. Clinical Psychology Review, 21, 1211-1226.

Birchwood,M., Spencer,E. & McGovern,D. (2000) Schizophrenia: early warning signs. Advances in Psychiatric Treatment, 6, 93-101.

Birchwood, M., Smith, J., Drury, V., Healy, J., Macmillan, F., & Slade, M. A. (1994). A self-report Insight Scale for psychosis: reliability, validity and sensitivity to change. Acta Psychiatrica Scandinavica, 89, 62-67.

Bock, T. (2000). Psychosen zonder psychiatrie (Psychosis without psychiatry) Amsterdam: Candide.

Boevink,W.A., Wolf,J.R.L.M., Nieuwenhuizen,C. & Schene,A.H. (1995). Kwaliteit van leven van langdurig van ambulante zorg afhankelijke psychiatrische patienten; een conceptuele verkenning.[Quality of life of longterm care dependent psychiatric patients; a conceptual exploration]. Tijdschrift voor Psychiatrie, 2, 97-110.

Boker,W., Brenner,H.D. & Wurgler,S. (1989) Vulnerability-linked Deficiences, Psychopathology and Coping Behaviour of Schizophrenics and their Relatives. Br.J.Psychiatry, 155, 128-135.

Bordin, E. S. (1976). The generalizability of the psychoanalytic concept of the working alliance. Psychotherapy: Theory, Research and Practice, 16, 252-260.

Bosch, R. J. v. d. (1993). Schizofrenie. Subjectieve ervaringen en cognitief onderzoek (Schizophrenia: subjective experiences and cognitive research). Groningen: Bohn Stafleu Van Loghum.

Breier,A. & Strauss,J.S. (1983) Self-control in Psychotic Disorders. Arch.Gen.Psychiatry, 40, 1141-1145.

Bromet, E. J. & Fennig, S. (1999). Epidemiology and Natural History of Schizophrenia. Biological Psychiatry, 46, 871-881.

Buchanan,R.W. & Carpenter,W.T. (2000) Schizophrenia: Introduction and Overview. In B.J.Sadock et al. (Eds.), Comprehensive Textbook of Psychiatry (pp. 1096-1110). Philadelphia: Lippincott Williams & Wilkins.

Bustillo,J., Buchanan,R.W. & Carpenter,W.T. (1995) Prodromal Symptoms vs. Early Warning Signs and Clinical Action in Schizophrenia. Schizophr.Bull., 4, 553-559.

Bustillo,J., Keith,S.J. & Lauriello, J. (2000) Schizophrenia: Psychosocial Treatment. In B.J. Sadock et al. (Eds.) Comprehensive Textbook of Psychiatry (pp. 1210-1217). Philadelphia: Lippincott Williams & Wilkins.

Campo,J. & Merckelbach,H. (1996) Schizofrene patiënten en haardracht [Schizophrenic Patients and hair cut]. Tijdschrift voor Psychiatrie, 9, 690-694.

Cancro, R. & Lehmann, H. E. (2000). Schizophrenia: Clinical Features. In B.J.Sadock & V. A. Sadock (Eds.), Comprehensive textbook of psychiatry (7 ed., pp. 1169-1199). Philadelphia: Lippincott Williams & Wilkins.

Carpenter,W.T., Hanlon,T.E., Heinrichs,D.W., Summerfelt,A.T., Kirkpatrick,B., Levine,J. & Buchanan,R.W. (1990) Continuous Versus Targeted Medication in Schizophrenic Outpatients: Outcome Results. Am.J.Psychiatry, 9, 1138-1148.

Carpenter,W.T. & Heinrichs,D.W. (1983) Early Intervention, Time Limited, Targeted Pharmacotherapy of Schizophrenia. Schizophr.Bull., 9, 533-542.

Carr,V. (1988) Patients' techniques for coping with schizophrenia: An exploratory study. British Journal of Medical Psychology, 61, 339-352.

Clinical Standards Board for Scotland (2002) Standards / Mental Health / Schizophrenia. www.clinicalstandards.org.

Cohen,C.I. & Berk,L.A. (1985) Personal Coping Styles of Schizophrenic Outpatients. Hospital and Community Psychiatry, 36, 407-410.

Crow,T.J., Macmillan,J.F., Johnson,A.L. & Johnstone,E.C. (1986) A randomised controlled trial of prophylactic neuroleptic treatment. Br.J.Psychiatry, 148, 120- 127.

David, A.S. (1990) Insight and Psychosis. Br.J.Psychiatry, 156, 798-808.

Dewettinck, I., Grypdonck, M. H. F., & Dhondt, A. (2001). Leven met vochtbeperking: een moeilijke opdracht [Living with fluid restriction: a difficult task]. TVZ Tijdschrift voor Verpleegkundigen, 111, 675-680.

Docherty,J.P., Kammen,D.P., Siris, S.G. & Marder,S.R. (1978) Stages of Onset of Schizophrenic Psychosis. Am.J.Psychiatry, 135, 420-426.

Eaton, W. W. (1985). Epidemiology of Schizophrenia. Epidemiologic Reviews, 7, 105-126.

Eaton, W. W. (1991). Update on the Epidemiology of Schizophrenia. Epidemiologic Reviews, 13, 320- 328.

Eckman, T. A., Wirshing, W. C., Marder, S. R., Liberman, R. P., Johnston-Cronk, K., Zimmerman, K., & Mintz, J. (1992). Technique for Training Schizophrenic Patients in Illness Self-Management: A Controlled Trial. American Journal of Psychiatry, 149, 1549- 555.

Evers,S.M.A.A., Wiersma,D. & Ament,A.J.H.A. (1995) Kosten van schizofrenie in Nederland [Costs of schizophrenia in The Netherlands]. In P.M.A.J.Dingemans et al.(Eds.), Schizofrenie. Onderzoek en implicaties voor de behandeling [Schizophrenia. Research and Implications for treatment] (pp. 290-299). Houten/Diegem: Bohn Stafleu Van Loghum.

Falloon,I.R.H. (1987) Cognitive and Behavioural Interventions in the Self Control of Schizophrenia. In Strauss et al. (Eds.) Psychosocial Treatment of Schizophrenia (pp. 180-190), Toronto: Hans Huber Publishers.

Gaag, M. van der., Bervoets, P., & Boer, K. de. (1994). Psychose Inzicht Schaal (Insight Scale /translation in Dutch / original author M. Birchwood et al. 1994).

Gaebel,W., Frick,U., Kopcke,W., Linden,M., Muller,P., Muller-Spahn,F., Pietzcker,A. & Tegeler,J. (1993) Early Neuroleptic Intervention In Schizophrenia: Are Prodromal Symptoms Valid Predictors of Relapse? Br.J.Psychiatry, 163 (suppl.21), 8-12.

Gaebel,W., Janner,M., Frommann,N., Pietzcker,A., Kopcke,W., Linden,M., Muller,P., Muller-Spahn,F. & Tegeler,J. (2002) First vs multiple episode schizophrenia: two-year outcome of intermittent and maintenance medication strategies. Schizophrenia Research, 53, 145-159.

Gamel, C., Grypdonck, M., Hengeveld, M., & Davis, B. (2001). A method to develop a nursing intervention: the contribution of qualitative studies to the process. Journal of Advanced Nursing, 33, 806-819.

Gamel, C. J. (2000). Sexual Health Care After Cancer Diagnosis: Development of a nursing intervention provided during the early recovery period after treatment for gynaecological cancer (PhD-thesis). Royal Library, The Hague.

Gilbert,P.L., Harris,M.J., McAdams,L.A. & Jeste,D.V. (1995) Neuroleptic withdrawal in schizophrenic patients. A review of the literature. Arch.Gen.Psychiatry, 52, 173-188.

Glazer, W.M. & Ereshefsky, L (1996). A pharmacoeconomic model of outpatient antipsychotic therapy in "revolving door" schizophrenic patients. J-Clin-Psychiatry, 57, 337-345.

Glazer, W.M. (1996). The impact of managed care systems on relapse prevention and quality of life for patients with schizophrenia. Eur. Neuropsychopharmacol., 6 Suppl 2: S35-39.

Goulet, J., Lalonde, P., Lavoie, G., & Jodoin, F. (1993). [Effect of patient education on neuroleptic treatment of young psychotic patients]. Can.J.Psychiatry, 38, 571- 573.

Guy, W. (1976). ECDEU Manual of Rating Scores and Instruments (USDHEW-ADAMHA-NIMH Publ. No. (ADM) 76-338. Washington DC: Superintendent of Documents US Government Printing.

Haan, R. J. d., Semin-Goossens, A., Lindeboom, R., & Vos, R. d. (1998). Verpleegkundig interventie-onderzoek. Een methodologische en statistische beschouwing (Intervention studies in nursing. Methodological and statistical considerations). Verpleegkunde, 13, 261-267.

Haro, J.M., Salvador-Carulla,L., Cabases, J., Madoz, V. & Vazquez-Barquero, J.L. (1998). Utilisation of mental health services and costs of patients with schizophrenia in three areas of Spain. Br-J-Psychiatry. Oct; 173: 334-340.

Hegarty, J. D., Baldessarini, R. J., Tohen, M., Waternaux, C., & Oepen, G. (1994). One Hundred Years of Schizophrenia: A Meta-Analysis of the Outcome Literature. American Journal of Psychiatry, 151, 1409-1416.

Hamera,E., Peterson,K.A., Young,L.M. & McNary Schaumloffel,M. (1992) Symptom Monitoring in Schizophrenia: Potential for Enhancing Self-Care. Archives of Psychiatric Nursing, 6, 324-330.

Heinrichs,D.W. & Carpenter,W.T. (1985) Prospective Study of Prodromal Symptoms in Schizophrenic Relapse. Am.J.Psychiatry, 3, 371-373.

Heinrichs,D.W., Cohen,B.P. & Carpenter,W.T. (1985) Early Insight and the Management of Schizophrenic Decompensation. The J.of Nerv.and Mental Disease, 3, 133-138.

Henmi,Y. (1993) Prodromal Symptoms of Relapse in Schizophrenic Outpatients: Retrospective and Prospective Study. The Jpn. J.of Psychiatry and Neurology, 4, 753-775.

Hert,M.A.F.d. & Slooff,C.J. (2000) Psychopharmacologische behandeling van schizofrenie en aanverwante psychosen [Psychopharmacological treatment of schizophrenia and related psychoses. In G. Pieters et al. (Eds.) Rehabilitation strategies for schizophrenia and longterm dependent patients] (pp 70-84), Houten/Diegem: Bohn Stafleu Van Loghum.

Herz,M.I., Glazer,W., Mirza,M., Mostert,M. & Hafez,H. (1989) Treating Prodromal Episodes to Prevent Relapse in Schizophrenia. Br.J.Psychiatry, 155(suppl.5), 123-127.

Herz,M.I., Glazer,W.M., Mostert,M.A., Sheard,M.A., Szymanski,H.V., Hafez,H., Mirza,M. & Vana,J. (1991) Intermittent vs Maintenance Medication in Schizophrenia. Arch.Gen.Psychiatry, 48, 333-339.

Herz,M.I. & Lamberti,J.S. (1995) Prodromal Symptoms and Relapse Prevention In Schizophrenia. Schizophr.Bull., 4, 541-551.

Herz,M.I. & Melville,C. (1980) Relapse in Schizophrenia. Am.J.Psychiatry, 7, 801-805.

Herz,M.I., Szymanski,H.V. & Simon,J.C. (1982) Intermittent Medication for Stable Schizophrenic Outpatients: An Alternative to Maintenance Medication. Am.J.Psychiatry, 139(7), 918-922.

Herz, M. I., Lamberti, J. S., Mintz, J., Scott, R., O'Dell, S. P., McCartan, L., & Nix, G. 2000). A Program for Relapse Prevention in Schizophrenia: A Controlled Study. Archives of General Psychiatry, 57, 277-283.

Hirsch,S.R. & Jolley,A.G. (1989) The Dysphoric Syndrome in Schizophrenia and its Implications or Relapse. Br.J.Psychiatry, 155(suppl.5), 46-50.

Holmes, H., Ziemba, J., Evans, T. & Williams, C. A (1994) Nursing Model of Psychoeducation for the Seriously Mentally Ill Patient. Issues in Mental Health Nursing, 15, 85-104.

Horvath, A. O. & Greenberg, L. S. (1989). Development and Validation of the Working Alliance Inventory. Journal of Counseling Psychology, 36, 223-233.

Inderbitzin,L.B., Lewine,R.R.J., Scheller-Gilkey,G., Swofford,C.D., Egan,G.J., Gloerson, B.J., Vidanagama,B.P. & Waternaux,C. (1994) A Double-Blind Dose- Reduction Trial of Fluphenazine Decanoate for Chronic Unstable Schizophrenic Patients. Am.J.Psychiatry, 151, 753-1759.

Jablensky, A. (1995). Schizophrenia: the Epidemiological Horizon. In S.R.Hirsch & D. R. Weinberger (Eds.), Schizophrenia (pp. 206-252). Blackwell Science.

Jenny, J. & Logan, J. (1991). Analyzing Expert Nursing Practice to Develop a New Nursing Diagnosis: Dysfunctional Ventilatory Weaning Response. In Classification of nursing diagnoses. Lippincott, Philadelphia. pp. 133-140.

Jolley,A.G., Hirsch,S.R., Morrison,E., McRink,A. & Wilson,L. (1990) Trial of brief intermittent neuroleptic prophylaxis for selected schizophrenic outpatients: clinical and social outcome at two years. British Medical Journal, 301, 837-842.

Jorgensen,P. (1998): Early signs of psychotic relapse in schizophrenia. Br.J.Psychiatry, 172, 327-330.

Joseph, J. F. d., Norbeck, J. S., Smith, R. T., & Miller, S. (1996). The development of a Social Support Intervention Among African American Women. Qualitative Health Research, 6, 283-297.

Kane, J.M. et al. (1998). Guidelines for depot antipsychotic treatment in schizophrenia. European Neuropsychopharmacology Consensus Conference in Siena, Italy. Eur-Neuropsychopharmacol. Feb, 8, 55-66

Kane, J.M. (1999). Management strategies for the treatment of schizophrenia. J.Clin. Psychiatry, 60 Suppl 12, 13-17.

Kay, S. R., Opler, L. A., & Fiszbein, A. (1987). Positive and Negative Syndrome Scale (PANSS) rating manual. San Rafael California: Social and Behavioral Sciences Documents.

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome rating scale (PANSS) for schizophrenia. Schizophrenia Bulletin, 13, 261-276.

Kennedy,M.G., Schepp,K.G. & O'Connor,F.W. (2000) Symptom Self-Management and Relapse in Schizophrenia. Archives of Psychiatric Nursing, 14, 266-275.

Kissling,W. (1991) Guidelines for Neuroleptic Relapse Prevention in Schizophrenia. Heidelberg: Springer-Verlag.

Kissling,W. (1992) Ideal and Reality of Neuroleptic Relapse Prevention. Br.J.Psychiatry, 161 (suppl.18), 133-139.

Kissling, W. & Leucht, S. (1999). Results of treatment of schizophrenia: is the glass half full or half empty? Int. Clin. Psychopharmacol., 14 Suppl 3: S11-4.

Kolk, N. (2003). Leven als partner van een afasiepatient (Living as a partner of a patient with aphasia). Thesis Nursing Science , University Utrecht.

Kumar,S., Thara,R. & Rajkumar,S. (1989) Coping with Symptoms of Relapse in Schizophrenia. Eur. Arch. Psychiatr. Neurol. Sci, 239, 213-215.

Levin, R. & Daly, R. S. (1998). Nightmares and Psychotic Decompensation: A Case Study. Psychiatry, 61, 217-222.

Liberman,R.P. & Kopelowicz,A. (1995) Basic elements in biobehavioral treatment and rehabilitation of schizophrenia. International Clinical Psychopharmacology, 9, 51-58.

Linszen,D., Dingemans,P., Does,J.W.v.d., Nugter,A., Scholte,P., Lenior,R. & Goldstein,M.J. (1996) Treatment, expressed emotion and relapse in recent onset schizophrenic disorders. Psychol.Med., 26, 333-342.

Linszen, D. H. (1993). Recent onset schizophrenic disorders. Outcome, prognosis and treatment. University of Amsterdam (PhD-thesis).

Lovejoy, M. (1984). Recovery from schizophrenia: a personal odyssey. Hospital and Community Psychiatry, 35, 809-812.

Malla,A.K. & Norman,R.M.G. (1994) Prodromal Symptoms in Schizophrenia. Br.J.Psychiatry, 164, 487-493.

Malla,A.K. & Norman,R.M.G. (1994) Prodromal symptoms in schizophrenia: A prospective investigation. Br.J.Psychiatry, 164, 487-493.

Marder,S.R., Mintz,J., Putten,T., Lebell,M., Wirshing,W.C. & Johnston-Cronk,K. (1991) Early prediction of relapse in schizophrenia: An application of receiver operating characteristics (ROC) methods. Psychopharmacology Bulletin, 27, 79-82.

Marder,S.R., Wirshing,W., Putten,T.v., Mintz,J., McKenzie,J., Johnston-Cronk,K., Lebell,M., Liberman,R.P. & Putten,T.v. (1994) Fluphenazine vs Placebo Supplementation for Prodromal Signs of Relapse in Schizophrenia. Arch.Gen.Psychiatry, 51, 280-287.

Marder, S. R., Wirshing, W. C., Mintz, J., McKenzie, J., Johnston, K., Eckman, T. A., Lebell, M., Zimmerman, K., & Liberman, R. P. (1996). Two-year outcome of social skills training and group psychotherapy for outpatients with schizophrenia. American Journal of Psychiatry, 153, 1585-1592.

Masand, P.S. & Berry, S.L.(2000). Switching antipsychotic therapies. Ann.Pharmacotherapy, 3, 200-207.

McCandless-Glimcher,L., McKnight,S., Hamera,E., Smith,B.L., Peterson,K.A. & Plumlee,A.A. (1986) Use of Symptoms of Schizophrenics to Monitor and Regulate their Illness. Hospital and Community Psychiatry, 37, 929-933.

McEvoy,J.P., Freter,S., Everett,G., Geller,J.L., Appelbaum,P., Apperson,L.J. & Roth,L. (1989)Insight and the Clinical Outcome of Schizophrenic Patients. The J.of Nerv.and Mental Disease, 1, 48-51.

McEvoy, J. P., Apperson, L. J., Ortlip, P. A., Brecosky, J., Hammill, K., Geller, J. L., Roth, L., & Ortlip, P. A. (1989a). Insight in Schizophrenia. Its Relationship to Acute Psychopathology. The Journal of Nervous and Mental Disease, 1, 43-47.

McGlashan, T. H. & Hoffman, R. E. (2000). Schizophrenia: Psychodynamic to Neurodynamic Theories. In B.J.Sadock & V. A. Sadock (Eds.), Comprehensive Textbook of Psychiatry (7 ed., pp. 1159-1169). Philadelphia: Lippincott Williams & Wolkins.

Meijel, B. v. (1996). De vroegtijdige onderkenning van prodromale verschijnselen bij patienten met schizofrenie [Early recognition of prodromal symptoms in patients with schizophrenia]. Verpleegkunde, 11 , 195-204.

Meijel,B.v. & Lendemeijer,B. (1997): Ziekte-inzicht bij patienten met schizofrenie [Insight in patients with schizophrenia]. TVZ, 8, 228-232.

Meijel, B. v., Gaag, M. v. d., Grypdonck, M., & Kahn, R. S. (2000). Protocol voor het werken met een signaleringsplan ter preventie van psychosen bij patienten met schizofrenie.[Protocol for working with relapse prevention plans in patients with schizophrenia]. Department of Nursing Science, Utrecht University.

Meijel, B. v., Gaag, M. v. d., Kahn, R. S., & Grypdonck, M. (2002a). Recognition of early warning signs in patients with schizophrenia: A review of the literature (submitted)

Meijel,B.v., Gaag,M.v.d., Kahn,R.S. & Grypdonck,M. (2002b): The practice of early recognition and early intervention to prevent psychotic relapse in patients with schizophrenia: an exploratory study. Part 1. Journal of Psychiatric and Mental Health Nursing, 9, 347-356.

Meijel,B.v., Gaag,M.v.d., Kahn,R.S. & Grypdonck,M. (2002c) The practice of early recognition and early intervention to prevent psychotic relapse in patients with schizophrenia: an exploratory study. Part 2. Journal of Psychiatric and Mental Health Nursing, 9, 357-364.

Meijel, B. v., Gaag, M. v. d., Kahn, R. S., & Grypdonck, M. (2002d). Relapse prevention in patients with schizophrenia: The development of a nursing intervention protocol Accepted: Archives of Psychiatric Nursing.

Meijel, B. v., Grypdonck, M. H. F., Gamel, C., & Swieten-Duijfjes, B. (2002e). The development of evidence based clinical interventions: methodological considerations. (submitted).

Mierlo,F.v. (1997) Vroege voortekenen van een psychose. [Early warning signs of psychosis] Utrecht: Trimbosinstitute.

Morse, J. M., Penrod, J., & Hupcey, J. E. (2000). Qualitative Outcome Analysis: Evaluating Nursing Intervention for Complex Clinical Phenomena. Journal of Nursing Scholarship, 32, 125-130.

Murdaugh, C. & Sowell, R. (1999). Developing a research based intervention to decrease perinatal HIV transmission. 11th International Nursing Research Congress 'Nursing Research: Defining the Future'. London UK, june26 (abstract).

Murphy,M.F. & Moller,M. (1993) Relapse Management in Neurobiological Disorders: The Moller-Murphy Symptom Management Assessment Tool. Archives of Psychiatric Nursing, 7, 226-235.

Narayanasamy, A. & Owens, J. (2001). A critical incident study of nurses' responses to the spiritual needs of their patients. Journal of Advanced Nursing, 33, 446-455.

Norman,R.M.G. & Malla,A.K. (1995) Prodromal Symptoms of Relapse in Schizophrenia: A Review. Schizophr.Bull., 4, 527-539.

Novacek, J. & Raskin, R (1998) Recognition of Warning Signs: A Consideration for Cost-Effective Treatment of Severe Mental Illness. Psychiatric Services, 49, 376-378.

Nuechterlein,K.H. & Dawson,M.E. (1984) A Heuristic Vulnerability/Stress Model of Schizophrenic Episodes. Schizophr.Bull., 10, 300-312.

Nuechterlein,K.H., Dawson,M.E., Gitlin,M., Ventura,J., Goldstein,M.J., Snyder,K.S., Yee,C.M. & Mintz,J. (1992) Developmental Processes in Schizophrenic Disorders: Longitudinal Studies of Vulnerability and Stress. Schizophr.Bull., 18, 387-425.

Nuechterlein,K.H., Dawson,M.E., Ventura,J., Gitlin,M., Subotnik,K.L., Mintz,J. & Bartzokis,G. (1994) The vulnerability / stress model of schizophrenic relapse: a longitudinal study. Acta Psychiatr.Scand., 89, 58-64.

O'Connor,F.W. (1991) Symptom Monitoring for Relapse Prevention in Schizophrenia. Archives of Psychiatric Nursing, 5, 193-201.

O'Connor, S. E. (2000). Nursing interventions in stroke rehabilitation: a study of nurses' views of their pattern of care in stroke units. Rehabilitation Nursing, 25, 224-230.

Oel,C.J., Hoek,H.W. & Kahn,R.S. (1994) Genetische epidemiologie van schizofrenie [Genetic epidemiology of schizophrenia] . Tijdschrift voor Psychiatrie, 10, 702-713.

Pietzcker,A., Gaebel,W., Kopcke,W., Linden,M., Muller,P., Muller-Spahn,F. & Tegeler,J. (1993) Intermittent versus maintenance neuroleptic long-term treatment in schizophrenia -2- year results of a German multicenter study. Journal of Psychiatric Research, 27, 321-339.

Rakel, B. A. (1992). Interventions related to patient teaching. Nursing Clinics of North America, 27, 397-422.

Ram, R., Bromet, E. J., Eaton, W. W., Pato, C., & Schwartz, J. E. (1992). The natural course of schizophrenia: a review of first-admission studies. Schizophrenia Bulletin, 18, 185-207.

Ream, E. & Richardson, A. (1999). From Theory to Practice: Designing Interventions to Reduce Fatigue in Patients With Cancer. Continuing Education, 26, 1295-1303.

Rice, D. P. (1999) The Economic Impact of Schizophrenia. Journal of Clinical Psychiatry, 60, 4-6.

Schene, A. H. & Wijngaarden, B. v. (1995). Consequenties voor het gezin en op het gezin gerichte interventies (consequences for the family and family-directed interventions). In P.M.A.J.Dingemans, R. J. v. d. Bosch, R. S. Kahn, & A. H. Schene (Eds.), Schizofrenie. Onderzoek en implicaties voor de behandeling (Schizophrenia: research and implications for treatment). (pp. 215-234). Houten: Bohn Stafleu Van Loghum.

Schooler,N.R., Keith,S.J., Severe,J.B. & Matthews,S.M. (1995) Maintenance Treatment of Schizophrenia: A Review of Dose Reduction and Family Treatment Strategies. Psychiatr.Q., 66, 279-292.

Schooler,N.R., Keith,S.J., Severe,J.B. et al. (1997) Relapse and Rehospitalization During Maintenance Treatment of Schizophrenia. Arch.Gen.Psychiatry, 54, 453-463.

Shaw, K., McFarlane, A., & Brookless, C. (1997). The Phenomenology of Traumatic Reactions to Psychotic Illness. The Journal of Nervous and Mental Disease, 185, 434-441.

Shepherd,M., Watt,D., Falloon,I. & Smeeton,N. (1989) The natural history of schizophrenia: a five year follow-up study of outcome and prediction in a representative sample of schizophrenics. Psychol.Med., 146-151.

Stenberg,J.H., Jaaskelainen,I.P. & Royks,R. (1998) The effect of symptom self-management training on rehospitalization for chronisc schizophrenia in Finland. International Review of Psychiatry, 58-61.

Struthers, J. (1999). An investigation into community psychiatric nurses' use of humour during client interactions. Journal of Advanced Nursing, 29, 1197-1204.

Subotnik,K.L. & Nuechterlein,K.H. (1988) Prodromal Signs and Symptoms in Schizophrenic Relapse. J.Abnorm.Psychol., 97, 405-411.

Swieten-Duijfjes, B. (1998). Ouderparticipatie bij kinderen met een chronische ziekte [Parental participation in chronically ill children]. Verpleegkunde, 13, 76-86.

Tarrier,N., Borrowclough,C. & Bamrah,J.S. (1991) Prodromal signs of relapse in schizophrenia. Social Psychiatry and Psychiatric Epidemiology, 26, 157-161.

Tarrier, N. (1997). Family Interventions and Schizophrenia. In G.Haddock & P. D. Slade (Eds.), Cognitive-Behavioural Interventions with Psychotic Disorders (pp. 212-234). London: Routledge.

Vervaecke, G. & Vertommen, H. (1993). De werkalliantie: visies op een bruikbaar concept en de meting ervan. Tijdschrift voor Psychotherapie, 19, 2-16.

Viguera,A.C., Baldessarini,R.J., Hegarty,J.D., Kammen,D.P. & Tohen,M. (1997) Clinical risk following abrupt and gradual withdrawal of maintenance neuroleptic treatment. Arch.Gen.Psychiatry , 54, 49-55.

Vlaminck, P. (2002). De schizofrenie ontmanteld (Schizophrenia dismantled). Maandblad Geestelijke volksgezondheid, 57, 342-363.

Vliet, M. J. v. (2001). Psychologische voorbereiding op een gastroscopie. De invloed van informatie in medische situaties [Preparing patients for gastrointestinal endoscopy. The influence of information in medical situations] (PhD-thesis). Academia Press, Ghent.

Vries,M.W.d. & Delespaul,Ph. (1988) Variabiliteit in schizofrenie symptomatologie [Variability in schizophrenic symptomatology]. In R.J. van den Bosch et al. (Eds.) Schizofrenie: recente ontwikkelingen in onderzoek en behandeling [Schizophrenia: recent developments in research and treatment] (pp. 203-228), Deventer: Van Loghum Slaterus.

Walker, L. O., Sandor, M. K., & Sands, D. (1989). Designing and Testing Self Help Interventions. Applied Nursing Research, 2, 96-99.

Wallace, C. J., Liberman, R. P., MacKain, S. J., Blackwell, G., & Eckman, T. A. (1992). Effectiveness and Replicability of Modules for Teaching Social and Instrumental Skills to the Severe Mentally ill. American Journal of Psychiatry, 149, 654-658.

Wallace, C. J. & Liberman, R. P. (1995). Social Skills Training for Patients With Schizophrenia: A Controlled Clinical Trial. Psychiatry Research, 15, 239-247.

Weiden, P.J. & Olfson, M. (1995). Cost of relapse in schizophrenia. Schizophr-Bull., 21, 419-429.

Westacott,M. (1995) Strategies for Managing Auditory Hallucinations. Nurs.Times, 3, 35-37.

Wiersma, D., Nienhuis, F. J., Giel, R., Jong, A., & Slooff, C. J. (1995). Schizofrenie en verwante psychotische stoornissen: het 15-jaars beloop van een incidentiecohort (Schizophrenia and related psychotic disorders: the 15 years course of an incidence cohort). Tijdschrift voor Psychiatrie, 9, 728-739.

Williams, R. & Dickson, R.A. (1995). Economics of schizophrenia. Can. J. Psychiatry. 40 (7 Suppl 2): S60-67.

Wing,J.K. (1978) The Social Context of Schizophrenia. Am.J.Psychiatry, 135, 1333-1339.

Wirshing, W. C., Eckman, T. A., Liberman, R. P., & Marder, S. R. (1991). Management of Risk of Relapse Through Skills Training of Chronic Schizophrenics. In C.A.Tamminga & S. C. Schulz (Eds.), Advances in Neuropsychiatry and Psychopharmacology. Volume 1: Schizophrenia Research. (pp. 255-267). New York: Raven Press.

Yank, G. R., Bentley, K. A., & Hargrove, D. S. (1993). The vulnerability-stress model of schizophrenia: Advances in psychosocial treatment. American Journal of Orthopsychiatry, 63, 55-69.

Zegwaard, M., Gamel, C., Duyvis, D. J., & Logmans, A. (2000). De beleving van seksualiteit en informatievoorziening van vrouw en partner na behandeling van cervixkanker [The experience of sexuality and information provision of women and their partners after treatment of a cervix carcinoma]. Verpleegkunde, 15, 18-28.

Ziekenfondsraad (1999). Farmacotherapeutisch Kompas (Pharmaco-therapeutical Compass). Amstelveen: Ziekenfondsraad.

Zubin,J. & Spring,B. (1977) Vulnerability. A new view of schizophrenia. J.Abnorm.Psychol., 86, 103-126.

Zubin, J., Steinhauer, S. R. &Condray, R. (1992) Vulnerability to Relapse in Schizophrenia. British Journal of Psychiatry, 161, 13-18.

Samenvatting

In dit proefschrift wordt verslag gedaan van een onderzoek naar de ontwikkeling en het testen van een verpleegkundige interventie gericht op de preventie van psychosen bij patiënten met schizofrenie of een aanverwante psychose. De interventie heeft als doel de vroegtijdige onderkenning van de voortekenen die optreden in de aanloopfase van een psychose. Wanneer deze vroegsignalering effectief geschiedt, kunnen tijdig acties worden uitgevoerd die de ontwikkeling van een ernstige psychotische crisis voorkomen en die bijdragen aan het evenwichtsherstel van de patiënt.

Na een inleidend ***hoofdstuk 1*** worden in ***hoofdstuk 2*** de resultaten van een literatuurstudie beschreven. Het hoofdstuk start met een beschrijving van het proces van psychotische decompensatie, van de allereerste voortekenen tot en met de psychotische crisis. De eerste voortekenen zijn veelal a-specifiek, zoals angst, onrust, lichte somberheid en concentratieproblemen. Zij gaan geleidelijk over in meer psychotisch getinte signalen, zoals toenemende achterdocht en milde hallucinaties. Birchwood *et al.* (1989) brengt de voortekenen onder in vier clusters: (1) angst / onrust (anxiety / agitation), (2) depressie / terugtrekgedrag (depression / withdrawal), (3) ontremming (disinhibition) en (4) beginnende psychose (incipient psychosis). Daarnaast zijn de zogenaamde idiosyncratische gedragingen van belang in het kader van vroegsignalering en vroege interventie. Het gaat hier om vreemde en excentrieke gedragingen van de patiënt die voor personen in de omgeving een onmiskenbaar signaal zijn dat de toestand van de patiënt aan het verslechteren is en dat een psychose dreigt.

De literatuur geeft aan dat het merendeel van de patiënten en/of de familieleden in staat is de voortekenen van een psychose adequaat te herkennen. Geconcludeerd wordt dat juist een gezamenlijke inspanning van patiënt, familieleden en hulpverleners een effectieve signalering bevordert.

Omtrent de voorspellende waarde van de vroege voortekenen is de literatuur niet erg eenduidig. De sensitiviteitswaarden liggen tussen de 8 en de 81%. Er worden verschillende oorzaken genoemd voor deze grote spreiding, die deels samenhangen met de methodologische opzet van deze studies en deels met de definiëring van de vroege voortekenen op basis waarvan de sensitiviteit is berekend. De specificiteitswaarden liggen tussen de 60 en 93%.

Geconcludeerd wordt dat de voorspellende waarde van vroege voortekenen kan toenemen, wanneer per patiënt een individueel profiel van voortekenen wordt opgesteld, hierbij uitgaande van een brede definitie van vroege voortekenen en met inclusie van eventuele idiosyncratische gedragingen.

In veel effectstudies worden methoden van vroegsignalering gecombineerd met uiteenlopende medicatiestrategieën. De waarde van de methoden van vroegsignalering zijn hier niet op zichzelf te beoordelen. Een beperkt aantal studies naar de effecten van vroegsignalering controleert voor medicatiegebruik. Zij geven aanwijzingen voor een toename van kennis en vaardigheden van de patiënt op het gebied van vroegsignalering en vroege interventie. Tevens tonen deze studies aan dat significante effecten worden bereikt met betrekking tot de preventie van psychotische terugval en het voorkomen van heropnamen.

De conclusie naar aanleiding van deze literatuurstudie is dat het beperkte interventie-onderzoek navolging verdient. Van bijzonder belang is het om de methoden voor vroegsignalering en vroege interventie verder te ontwikkelen. We concludeerden dat toepassing binnen de verpleegkundige praktijk een duidelijke meerwaarde kan hebben gezien het veelal frequente en intensieve contact tussen verpleegkundigen, patiënten en familieleden.

Hoofdstuk 3 gaat in op een aantal methodologische aspecten van interventie-ontwikkeling in de verpleegkunde. Het hoofdstuk opent met de stelling dat toetsing van de effectiviteit van interventies pas zinvol is nadat een zorgvuldig ontwikkelingstraject is doorlopen. Een model wordt gepresenteerd van de verschillende fasen binnen een dergelijk ontwikkelingstraject. De strategie van ontwikkeling wordt hierbij mede bepaald op basis van reeds beschikbare kennis die is geïnventariseerd in een literatuurstudie. Daaruit kan blijken dat er kennislacunes bestaan met betrekking tot de aard van het probleem waar de interventie zich op richt. Ook kan blijken dat de behoeften en zorgvragen van de patiënt onvoldoende bekend zijn. Dit kan aanleiding zijn tot deelstudies die tot beantwoording van deze vragen leiden. Tevens kunnen reeds bestaande interventiepraktijken worden bestudeerd, waar ervaring is opgedaan met het type interventie in kwestie. De onderzoeksdata uit deze bestaande praktijken kunnen bijdragen aan de verdere ontwikkeling en verfijning van de interventie.

Op basis van de gegevens uit het literatuuronderzoek, in combinatie met de resultaten uit eventueel uitgevoerde deelstudies, kan een eerste

ontwerp van de interventie worden opgesteld (Intervention Design). In de volgende fase van validering van de interventie (Intervention Validation) wordt dit eerste ontwerp op beperkte schaal – in case studies – toegepast in de (verpleegkundige) praktijk, waarbij de effecten op kwalitatieve wijze worden geëvalueerd. Naar aanleiding van deze evaluatie kan geleidelijke verfijning van (delen van) de interventie plaatsvinden.

Vervolgens kan eventueel effectonderzoek plaatsvinden middels een RCT (Randomised Controlled Trial). Het resultaat van dit ontwikkelingstraject is verpleegkundige interventie met een theoretische rationale voor de verschillende activiteiten die binnen de interventie worden uitgevoerd. Het traject maakt inzichtelijk welke effecten van deze activiteiten onder uiteenlopende condities mogen worden verwacht.

De ***hoofdstukken 4 en 5*** beschrijven vervolgens de resultaten van een exploratieve studie naar bestaande praktijken van vroegsignalering en vroege interventie. Het doel van deze studies was meer inzicht te verkrijgen in reeds toegepaste methoden van vroegsignalering en vroege interventie. Daarnaast richtte het onderzoek zich op de ervaringen van patiënten, familieleden en hulpverleners die zij opdeden met deze methoden. In totaal werden 25 kwalitatieve interviews uitgevoerd met respondenten uit 6 verschillende settings.

Er worden drie prototypische modellen beschreven van vroegsignalering en vroege interventie: (1) het basismodel (basic model), (2) het fasemodel (phase model) en (3) het omvattende model (comprehensive model). Er wordt beschreven hoe binnen deze praktijken de vroege voortekenen worden geïnventariseerd en uitgewerkt in zogenaamde signaleringsplannen (Relapse Prevention Plans). Tevens wordt inzicht geboden in de wijze van monitoring en scoring van de vroege voortekenen. Specifiek wordt ingegaan op de veelal prominente rol van familieleden en andere leden van het sociaal netwerk bij het opstellen van en het werken met een signaleringsplan.

De respondenten is gevraagd welke effecten zij waarnamen bij het werken met een signaleringsplan. Naast het voorkomen of uitstel van terugval, werden effecten genoemd als het beter kunnen verbaliseren van (pre-psychotische)ervaringen, angstreductie, vermindering van schuldgevoel door een beter begrip van de eigen situatie, en de mogelijkheid om goede afspraken te maken omtrent de verantwoordelijkheden van betrokkenen in tijden van dreigende crisis.

Vervolgens worden op basis van de interviews een aantal beïnvloedende factoren beschreven die de toepassing van methoden voor vroegsignalering bevorderen of juist belemmeren. Achtereenvolgens wordt ingegaan op de thema's (1) informatie en educatie, (2) de attitude van hulpverleners, (3) ziekte-inzicht van de patiënt, (4) ziekte-acceptatie, (5) motivatie, (6) een aantal andere patiëntkarakteristieken en (7) continuïteit van zorg.

Tot slot van beide hoofdstukken wordt een schematische opzet gepresenteerd van een interventieprotocol voor vroegsignalering en vroege interventie.

Deze schematische opzet wordt in ***hoofdstuk 6*** nader uitgewerkt. Uitgangspunt bij het ontwerp van het interventieprotocol was het kwetsbaarheid-stress-coping-model, zoals dit is beschreven door Nuechterlein *et al.* (1992). Na een beknopte uiteenzetting van dit model passeren een aantal uitgangspunten van het interventieprotocol de revue, die de basis vormen voor het opstellen van een op de individuele patiënt toegesneden signaleringsplan.

Vervolgens worden de structuur en de inhoud van het interventieprotocol beschreven. De activiteiten van de verpleegkundige worden uiteengezet in achtereenvolgens (1) de voorbereidingsfase, (2) de fase van het inventariseren en uitwerken van de vroege voortekenen, (3) de fase van monitoring van vroege voortekenen en (4) de fase van het opstellen van een actieplan, dat een integraal onderdeel vormt van het signaleringsplan. Het concept-protocol is ter validering voorgelegd aan een aantal experts op het gebied van schizofreniezorg. Tevens is het op bruikbaarheid (feasibility) getest in de verpleegkundige praktijk in een negental case studies. Dit leidde tot een beperkt aantal inhoudelijke aanpassingen van het interventieprotocol, evenals tot een aantal maatregelen die de toepasbaarheid in de reguliere verpleegkundige praktijk verder zouden kunnen bevorderen.

In de hoofdstukken 7 en 8 wordt gerapporteerd over het onderzoek naar de effecten van het interventieprotocol in een randomised controlled trial. Aan deze trial namen 48 verpleegkundigen (experimentele/ controlegroep: 26/22) en 95 patiënten (experimentele/controlegroep: 51/44) deel, afkomstig uit drie verschillende GGZ-organisaties. De verpleegkundigen in de experimentele groep ontvingen een training van twee dagdelen in de toepassing van het interventieprotocol, waarna zij met patiënten uit hun case

load een signaleringsplan opstelden. De verpleegkundigen in de controlegroep boden 'care as usual'. In een follow-up-periode van 1 jaar vond een systematische registratie plaats van psychotische terugvallen.

Hoofdstuk 7 beschrijft de resultaten van een schriftelijke enquête die gehouden is onder de verpleegkundigen die deelnamen aan de experimentele conditie binnen deze RCT. De enquête werd afgenomen op het moment dat de verpleegkundige, de patiënt en eventuele leden van het sociaal netwerk het opstellen van het signaleringsplan hadden afgerond. De enquête bevatte vragen en stellingen die inzicht boden in (1) de wijze waarop de verpleegkundigen feitelijk te werk waren gegaan bij de uitvoering van het interventieprotocol, (2) de ervaringen tijdens deze uitvoering en (3) de waardering voor het interventieprotocol.

De resultaten van deze enquête maken duidelijk dat de verpleegkundigen de globale structuur van het interventieprotocol betrekkelijk trouw volgden, maar dat zij er ook in slaagden hun concrete werkwijze zo aan te passen dat hiermee recht werd gedaan aan karakteristieken van de individuele patiënt en van zijn of haar sociaal netwerk. De enquête maakte tevens duidelijk dat bepaalde onderdelen van het interventieprotocol als moeilijk werden ervaren, waaronder de uitwerking van de vroege voortekenen in drie niveaus van ernst en het betrekken van familieleden bij bepaalde onderdelen van het signaleringsplan. De verpleegkundigen vermeldden verder dat voor een meerderheid van de patiënten het praten over eerdere psychosen een aanzienlijke belasting betekende en dat het voor 20% van hen zelfs negatieve stress-ervaringen opleverde. Deze laatste resultaten benadrukken de noodzaak van een goede dosering bij de uitvoering van de interventie.

Een ruime meerderheid van de verpleegkundigen oordeelde dat het opstellen van en het werken met het signaleringsplan een belangrijke bijdrage leverden aan de behandeling van de patiënt. Zij oordeelden optimistisch over de concrete toepassingsmogelijkheden van het werken met het signaleringsplan binnen de verpleegkundige begeleidingsrelatie, ook al ligt er voor de verpleegkundige een belangrijke taak in het actueel houden van de vroegsignalering binnen de behandeling.

Hoofdstuk 8 van dit proefschrift biedt in inzicht de kwantitatieve effecten van de interventie. Het terugvalpercentage in de experimentele groep bedroeg 12.5% versus 26.2% in de controlegroep. Dit verschil is niet significant ($X^2_{(1)}$=2.445; p=.12). Het Relatieve Risico van een psychose voor de patiënten in de controlegroep is ruim tweemaal zo groot als dat van de patiënten in de

experimentele groep (1/RR=2.095 / CI 95%: 0.79<X<5.0). Op een aantal secundaire uitkomstmaten (ziekte-inzicht, kwaliteit van de therapeutische alliantie en medicatiegebruik) werden geen significante of interpreteerbare verschillen tussen beide groepen gevonden.

Aan het slot van dit hoofdstuk worden de resultaten van de RCT nader beschouwd. Opvallend is dat het recidiefpercentage in de experimentele groep bijzonder laag is. De beschikbare literatuur laat zien dat een recidiefpercentage van 12.5% slechts wordt gevonden in studies waar optimale behandelcondities gelden. Echter, het recidiefpercentage in de controlegroep was eveneens bijzonder laag. De meeste studies geven onder 'care-as-usual' condities een recidiefpercentage van ongeveer 40%. Er worden verschillende verklaringen geponeerd voor het lage recidiefpercentage in de controlegroep, waaronder het contaminatie-effect, het Hawthorne-effect en een hogere kwaliteit van de reguliere zorg in Nederland.

Tot slot worden in ***hoofdstuk 9*** worden de resultaten van de verschillende deelstudies in hoofdlijnen samengevat en in hun onderlinge verband bediscussieerd.

Summary

This thesis describes a study into the development and testing of a nursing intervention with a view to preventing psychotic relapses in patients suffering from schizophrenia or a related disorder. The purpose of the intervention is to recognise the early signs of an oncoming psychotic relapse. If warning signs signalling the onset of a psychosis are adequately recognised at an early stage, action may be taken to prevent a serious psychotic episode and to help the patient regain his equilibrium.

Following a general introduction in ***Chapter 1***, ***Chapter 2*** describes the results of a literature review. It starts with an explanation of how a psychotic episode actually evolves, beginning with the very first warning signs and ending with the psychotic crisis. The first signs are often non-specific, varying from anxiety and agitation to gloominess and cognitive problems. These symptoms gradually advance to more psychotic signs, such as growing suspiciousness and mild hallucinations. Birchwood *et al.* (1989) divide the early signs into four categories: (1) anxiety / agitation; (2) depression / withdrawal; (3) disinhibition; and (4) incipient psychosis. Other signs that are relevant to early recognition and early intervention are the patient's own idiosyncrasies: strange and eccentric behavioural patterns which form an unmistakable indication for persons in the patient's social network to conclude that his situation is deteriorating and that he may have a psychosis.

The publications included in the literature review show that most of the patients and/or their families are well capable of recognising the early signs of a psychosis. The conclusion is that a joint effort by the patient, his family and the health care professionals will be conducive to an efficient recognition of early warning signs.

As for the predictive value of early symptoms, the publications are not very consistent. Sensitivity values are between 8 and 81%. There are various explanations for this wide range, for the one part relating to the methodological structure of the studies concerned and for the other part arising from the definition of the term 'early signs' as used for calculating the sensitivity. The specificity values range from 60 to 93%. The conclusion drawn in the thesis is that the predictive value of early signs may improve if an individual profile is made for each patient, with the concept of early signs being defined broadly and the patient's idiosyncrasies being taken into account.

Many studies into the effects of early recognition and early intervention combine early recognition methods and various medication strategies. It is impossible in this context to review these methods on their own merits. A limited number of studies into the effects of early recognition control for medication use. The studies generally indicate an increase in the patient's knowledge and skills in the fields of early recognition and early intervention. They also show that a significant effect can be achieved in terms of preventing psychotic relapses and re-admissions. The conclusion to be drawn from the literature review is that it is worthwhile continuing the limited research into these interventions. It is particularly important to work out the early recognition and early intervention methods in greater detail. Given the usually frequent and close contacts between nurses, patients and their families, the use of such methods will clearly have added value in nursing practice.

Chapter 3 focuses on a number of methodological aspects of developing interventions for nursing practice. It starts with the hypothesis that the effectiveness of interventions cannot be properly tested until a careful development procedure has been followed. Chapter 3 presents a model of the various stages to be included in such a development procedure. The development strategy is based in part on available knowledge taken from literature review. The conclusion drawn may then be that there is insufficient knowledge about the nature of the problem to be addressed by the intervention, or that the insight into the patients' needs and demands for care is insufficient. Such findings may lead to supplemental studies in which answers are to be found to these questions. Another option might be to study existing intervention practices, in which nurses have gained experience with the relevant type of intervention. Data on such practices may contribute to the further development and fine-tuning of interventions.

The data from the literature review and the results from specific supplemental studies that may have been conducted form the basis for preparing the first draft of the intervention (intervention design). Next, the intervention will have to be tested in (nursing) practice on a limited scale - in case studies - in the intervention validation stage, during which the effects of the intervention will be evaluated with qualitative research methods. The evaluation may give rise to a gradual fine-tuning of (elements of) the intervention. The next step may be an evaluation of effects by means of an RCT (Randomised Controlled Trial).

This overall development procedure will produce a practical intervention method with a theoretical rationale behind the various activities undertaken during the intervention.

Chapters 4 and 5 describe the results of an exploratory study into existing early recognition and early intervention practices. The study was carried out so as to gain a better understanding of the early recognition and early intervention methods that are already in place. In addition, the study focused on how patients, their families and health care professionals experienced those methods. A total of 25 qualitative interviews were held in six different settings.

Three models for early recognition and early intervention were distinguished: (1) the basic model; (2) the phase model; and (3) the comprehensive model. The study described how early warning signs were identified in these models and worked out in relapse prevention plans. It also explained the methods that were used to monitor and score early signs. Specific attention was paid to the often prominent role played by family members and other members of the patient's social network in preparing and working with a relapse prevention plan.

Respondents were asked about the effects they observed when working with a relapse prevention plan. Apart from the obvious effects of relapse prevention or a relapse delay, the most common effects mentioned were: an improved verbal expression of (pre-psychotic) experiences, reduced anxiety, a reduced feeling of guilt because of a better understanding of their own situation, and the opportunity to make a proper division of responsibilities in times of a pending crisis.

The study then used the interviews as a basis for identifying a number of factors that had an impact, whether positive or negative, on the early recognition methods employed. The following issues were addressed in this context: (1) information and education; (2) attitude of professionals; (3) the patient's insight into his disorder; (4) acceptance; (5) motivation; (6) other patient characteristics; and (7) continuity of care.

The two Chapters are concluded by a schematic presentation showing the outlines of an early recognition and early intervention protocol.

This schematic structure is worked out in greater detail in ***Chapter 6***. It is the vulnerability-stress-coping model as described by Nuechterlein *et al.* (1992) that was used as a basis for developing the intervention protocol.

Following a brief explanation of this model, Chapter 6 goes on to address a number of the basic assumptions that are to form the basis for preparing a relapse prevention plan specifically dovetailed to the patient in question, and then describes the structure and content of the intervention protocol. The focus is on the activities of nurses in the following four phases: (1) the preparatory phase; (2) the listing of early warning signs; (3) the monitoring of early signs; and (4) the phase of preparing an action plan, which forms an integral part of the relapse prevention plan.

The draft protocol was presented for validation to a number of experts in the field of schizophrenia care. It was also tested in nine case studies on feasibility in nursing practice. This led to a few substantive adjustments to the intervention protocol, and to a number of actions that may further enhance the protocol's applicability in nursing practice.

Chapters 7 and 8 report on research that was carried out into the effects of the intervention protocol by means of a randomised controlled trial (RCT). The trial was conducted with the aid of 48 nurses (experimental/control group: 26/22) and 95 patients (experimental/control group: 51/44) from three mental health care organisations. The nurses in the experimental group were trained during two half days on how to use the intervention protocol and were then instructed to prepare relapse prevention plans with patients from their case load. The nurses in the control group provided care as usual. The psychotic relapses among patients were registered systematically during the one-year follow-up period.

Chapter 7 describes the results of a survey among nurses who participated in the RCT in the experimental group. The nurses were asked to fill out a questionnaire after they and their patients had finished preparing the relapse prevention plan. The questionnaire included questions and positions that were to provide insight into (1) the way in which the nurses had applied the intervention protocol in actual practice; (2) the experiences gained from working with the intervention protocol; and (3) the appreciation of the intervention protocol.

The results of the survey showed that nurses generally followed the overall structure of the intervention protocol quite conscientiously, but that they were also able to adjust their working procedures in such a way as to do justice to the characteristics of the individual patients and their social networks. The survey also made it clear that specific elements of the

intervention protocol were considered difficult, including the elaboration of early signs into three levels of severity and the involvement of family members in specific phases of the relapse prevention plan. The nurses further reported that a majority of the patients found it stressful to discuss previous relapses and that 20% even suffered negative stress experiences. These findings in particular emphasise the need for a proper "dosage" of intervention.

A large majority of the nurses concluded that relapse prevention plans contributed greatly to the treatment of patients. They were optimistic about the practical application possibilities of working with a relapse prevention plan as part of their nursing relationship with the patients, although it would be important to ensure that early recognition was constantly kept up to date.

Chapter 8 of this thesis discusses the quantitative effects of intervention. The relapse percentage in the experimental group was 12.5% versus 26.2% in the control group. This difference is not significant ($X^2_{(1)}=2.445$; p=.12). The relative risk of a psychosis for patients in the control group was more than twice the risk rate for patients in the experimental group (1/RR=2.095 / CI 95%: 0.79<X<5.0). No significant or interpretable differences between the two groups could be discerned at the level of a number of secondary outcome variables (insight, quality of working alliance and use of anti-psychotic drugs).

The results of the RCT are analysed in greater detail at the end of Chapter 8. The most noticeable fact is the very low relapse rate in the experimental group. The publications evaluated show that a relapse rate of 12.5% only occurs in studies with optimal treatment conditions. On the other hand, the relapse rate in the control group was also very low. Most studies provide a figure of approximately 40% in care-as-usual conditions. Different explanations are suggested for the low relapse rate in the control group, including the contamination effect, the Hawthorne effect and the high level of 'care-as-usual' in the Netherlands.

Finally, ***Chapter 9*** summarises the results of the various studies that formed the basis for this thesis and discusses these results as a whole.

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Sinds ruim een jaar maakt Verplegingswetenschap deel uit van het Julius Centrum voor Gezondheidswetenschappen en Eerstelijns Geneeskunde. In mijn functie van adjunct-disciplinehoofd Verplegingswetenschap heb ik de afgelopen periode op zeer plezierige wijze samengewerkt met de leiding van de divisie. Ik wil het managementteam - bestaande uit prof. dr. D.E. Grobbee, prof. dr. B.A. van Hout, prof. dr. Th. Verheij en de heer P. Boerlage – hartelijk danken voor de inspanningen om de verplegingswetenschappers een goede plaats binnen de divisie te geven. Ook dank aan de mensen van het bedrijfsbureau die op zeer professionele wijze ondersteuning boden op financieel en personeelsgebied.

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Vreemd …

De stilte hier

Geeft me het gevoel

Dat je me hoort

(L. Spee)

Curriculum Vitae

Berno van Meijel was born in Delft, the Netherlands, on the 18th of August 1960. Having completed his pre-university education (VWO) in 1981, he went on to be trained as a nurse at a general hospital in Oldenzaal. Subsequently, from 1984 to 1987, he attended the Hogeschool Sittard, where he obtained his bachelor's degree in nursing. In the course of his education, he developed a special interest in mental health nursing; after his graduation, therefore, he continued his career at the Department of Psychiatry of the University Medical Centre Utrecht (UMCU), where he worked predominantly with patients suffering from eating and personality disorders. At the same time, he enrolled as a part-time student at the Faculty of Social Sciences of the Utrecht University to study Health Studies. He obtained his degree in 1991 and took up work as a researcher at the Netherlands Centre for Mental Health, currently known as the Trimbos Institute. He contributed to studies on mental health policy and organisational cooperation in mental health care. In 1993 he went back to the University Medical Centre Utrecht to start work as a staff member for the Board of Directors. As such he was especially charged with promoting nursing sciences within this organisation. One year later (1994) he had the opportunity to start his own Ph.D. research at the Department of Psychiatry and the Department of Nursing Sciences. During the first four years of his Ph.D. program, he combined his study with a job as a lecturer in nursing at the Hogeschool Amsterdam. In 1998 he accepted a full-time job at the Department of Psychiatry, from where he moved to the Department of Nursing Sciences in 2000. At the latter department he was also responsible for research coordination.

Following his Ph.D. program, Berno van Meijel will focus on research, innovation and education in the field of mental health nursing, both as a researcher at the Department of Nursing Science in Utrecht and as an associate professor in Mental Health Nursing at the INHOLLAND University (Alkmaar / Amsterdam).