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# Schizophrenia: early warning signs

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Relapse in schizophrenia remains common and cannot be entirely eliminated even by the best combination of biological and psychosocial interventions (Linszen *et al*, 1998). Relapse prevention is crucial as each relapse may result in the growth of residual symptoms (Shepherd *et al*, 1989) and accelerating social disablement (Hogarty *et al*, 1991). Many patients feel 'entrapped' by their illnesses, a factor highly correlated with depression (Birchwood *et al*, 1993), and have expressed a strong interest in learning to recognise and prevent impending psychotic relapse.

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## Early warning signs and the 'relapse signature'

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The 'early warning signs' approach to relapse prevention seeks to identify the earliest signs of impending psychotic relapse and to offer timely and effective intervention to arrest their progression towards frank psychosis.

### *What are the 'early warning signs' of psychotic relapse?*

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Investigations (e.g. Herz & Melville, 1980; Birchwood *et al*, 1989; Jørgensen, 1998) have consistently determined that subtle changes in thought, affect and behaviour precede development of frank psychosis.

'Dysphoric' symptoms (depressed mood, withdrawal, sleep and appetite problems) are most commonly reported, while psychotic-like symptoms (for example, a sense of being laughed at or talked about) are less frequent. Furthermore, these symptoms generally occur in a predictable order, with non-psychotic phenomena occurring early in the illness, followed by increasing levels of emotional disturbance and, finally, by the development of frankly psychotic symptoms (Docherty *et al*, 1978). The progression occurs, most frequently, over a period of less than four weeks (Birchwood *et al*, 1989; Jørgensen, 1998).

Although these symptoms have sometimes been referred to as the psychotic 'prodrome', they are more accurately conceptualised as 'early warning signs' of psychotic relapse, since the concept of a 'prodrome' (a term derived from the medical literature) implies a disease progression that cannot be interrupted. However, investigators have found that people with psychosis actively use coping strategies to intervene in the onset of psychosis (McCandless-Glimcher *et al*, 1986). Furthermore, strictly speaking, 'prodromal' symptoms of psychosis include only those non-specific symptoms that may signal the onset of a variety of illnesses. However, attempts to predict the onset of psychosis from non-specific or dysphoric prodromal symptoms alone have yielded poor sensitivities and/or specificities (e.g. Jolley *et al*, 1990), but results have been more promising when low-level psychotic symptoms are included in the predictor variables.

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## Can psychotic relapse be predicted accurately from these early warning signs?

Prospective studies (Subotnik & Neuchterlein, 1988; Birchwood *et al*, 1989; Jørgenson, 1998) have shown that psychotic relapse can be predicted with a sensitivity of 50–79% and a specificity of 75–81% when standardised measures of ‘neurotic’ or ‘dysphoric’ symptoms are combined with those of low-level psychotic symptoms and ratings are conducted at least fortnightly.

However, there is considerable variability between individuals in the nature and timing of their early warning signs (Birchwood *et al*, 1989), and prediction of relapse is more accurate if changes in early warning scores are evaluated against individuals’ own baseline scores rather than compared with those of other patients (Subotnik & Neuchterlein, 1988; Jørgensen, 1998). Thus, to be clinically useful, methods of identifying early warning signs of psychotic relapse must take into account this individual variation.

For these reasons, research attention has recently been directed towards identifying and managing each patient’s ‘relapse signature’ (Birchwood, 1995): his or her unique pattern of early warning signs most likely to indicate impending psychotic relapse. Later in this article, we will present a methodology used in our clinical practice for this purpose.

## Can patients identify their own early warning signs?

A large percentage of people with schizophrenia and their relatives are aware of these early signs of impending relapse (Herz & Melville, 1980). One study found that 63% of patients maintained insight into their deteriorating mental state until the day of their relapse (Heinrichs *et al*, 1985). Jørgensen (1998) also found that patient self-reports of early warning signs predicted relapse with a sensitivity and a specificity almost equal to those derived from psychiatrists.

## Interventions following the early warning signs

In our practice, two sorts of interventions are offered following the onset of early warning signs: cognitive–behavioural therapy and medication.

## Cognitive–behavioural interventions

The ‘stress–vulnerability model’ (Zubin & Spring, 1977) views the symptoms of schizophrenia as the result of environmental stressors acting on the vulnerable individual, and predicts that a reduction in stress or the acquisition of stress management skills should decrease the chance of psychotic relapse. The association of stressful life events (Hirsch *et al*, 1996) and stressful home environments (Kuipers & Bebbington, 1988) with relapse among people with schizophrenia adds weight to this model and its predictions.

There is evidence that even after the onset of early warning signs, stress management skills may be helpful in preventing psychotic relapse. For example, McCandless-Glimcher *et al* (1986) found that many patients with schizophrenia use cognitive–behavioural techniques to deal with the early warning signs of relapse without being formally instructed to do so. Furthermore, Hogarty *et al* (1997) found that treatment with an individualised and graded approach to stress management, particularly focusing on the identification and management of affective dysregulation preceding relapse (‘personal therapy’), was associated with a significant overall effect in delaying adverse events (including psychotic or affective relapse or treatment-related termination) relative to supportive therapy, for patients living with their families.

A second strand of cognitive therapy focuses on the meanings with which patients invest their symptoms and the evidence that they hold for their beliefs. Therapeutic techniques within this framework have been evaluated in frank psychosis and found to result in statistically significantly greater improvements in psychotic symptoms relative to control conditions (Garety *et al*, 1994; Drury *et al*, 1996a). Furthermore, depending on the definition of recovery used, cognitive therapy has been found to reduce time of recovery from psychosis by 25–50% (Drury *et al*, 1996b). These successes have encouraged an extension of the theoretical concepts underlying these techniques to the early warning sign period. Birchwood (1995), for example, proposes that early warning signs may represent symptoms intrinsic to the illness combined with a psychological response that centres on a search for meaning and control, which may, in turn, contribute to whether the relapse is arrested or accelerated. Psychological responses involving denial or excessive fear of relapse are hypothesised to be internal stressors, which, in themselves, increase the probability of relapse. Cognitive therapy techniques that challenge these dysfunctional beliefs may thus prevent the escalation of early warning signs to frank psychosis.

## Medication

Intermittent medication initiated only at detection of early warning signs has been shown to be inferior to continuous medication in preventing psychotic relapse and is not generally recommended (Carpenter *et al*, 1990; Gaebel *et al*, 1993). However, medication initiated on the development of early warning signs in combination with maintenance medication has been shown to reduce psychotic relapse rates to 12–23% over two years (Marder *et al*, 1984, 1987; Jolley *et al*, 1990; Gaebel *et al*, 1993). Furthermore, in most cases this strategy has allowed a low maintenance dose of medication to be successfully used. Marder *et al* (1994), for example, demonstrated a significant reduction in the risk of relapse and time spent in psychosis from the second year of treatment with a combination of low-dose maintenance medication plus medication targeted at early warning signs, when compared with treatment with low-dose maintenance medication only.

## Construction of the relapse signature and drill

The above considerations have stimulated the development of a structured methodology for the identification and management of individual relapse signatures, known as the 'back in the saddle' (BITS) approach to relapse prevention (further details available from the author upon request). This approach involves five stages (see Box 1).

### Engagement and education

The identification of the relapse signature and drill forms an ideal medium through which to establish common ground with the patient and to acknowledge his or her point of view.

Initial sessions focus on understanding the individual's attitude towards his or her illness, especially his or her perception of the risk and controllability of relapse. Beliefs that may exacerbate the relapse process, for example, poor perceived control over the illness causing the individual to panic or fail to act on the occurrence of early signs, are identified.

It is suggested to the patient and his or her family that fear of relapse may be coped with through skill-learning, and the analogy of a 'safety net' is used to describe these skills. Such a discussion draws upon the positive steps already being taken by the individual to remain well, and occurs in the context of general psychoeducation concerning preventable risk factors

### Box 1. Managing the early warning signs of schizophrenia

Engagement and education  
 Identification of the relapse signature  
 Development of a relapse drill  
 Rehearsal and monitoring  
 Clarification of the relapse signature and drill

of psychotic relapse (e.g. discontinuation of medication and illicit drug use). An example of a completed relapse prevention sheet is shown (see Boxes 2a,b).

### Identification of the relapse signature

The aim of the next part of the process is to construct a hypothesis about the individualised relapse signature: that is, a set of general and idiosyncratic symptoms, occurring in a specific order, over a particular time period, that serve as early warning signs of impending psychotic relapse.

Patients are first introduced to examples of early warning signs of psychotic relapse. They are then encouraged to review, either alone or with the support of their keyworker or family, any noticeable changes in their thoughts, perceptions, feelings and behaviours leading up to their most recent episode of illness, as well as any events that they think may have triggered these.

Two structured exercises are then used to expand and order this set of early warning signs.

#### Time line exercise

The individual is supported in constructing a time line of significant external events, proceeding backwards in time from the date of referral to mental health services. These events may include activities, special events, weather conditions and current affairs. Early warning signs that the patient identified in the previous part of the process are 'pegged' to these external events, and the latter are also used as retrieval cues to further expand on the changes in thoughts, feelings and behaviours that the patient experienced in the lead-up to the onset of their recent psychotic episode.

#### The card sort exercise

Similarly, 55 cards describing non-specific and psychotic symptoms, constituting early warning signs of psychotic relapse drawn from the empirical literature, are presented to the patient (see Box 3).

**Box 2a. Relapse prevention sheet**

Name: PF

Date:

*Relapse signature*

Increased feelings of inadequacy  
 Preoccupied about self-improvement,  
 including constantly monitoring  
 yourself for faults  
 Increased feelings of anxiety  
 and restlessness

## Racing thoughts/intrusive thoughts

Feelings of elation/spirituality  
 Do not need to sleep (one night or more)  
 Suspicious of people close to you  
 Not wanting to eat

## Horroric thoughts and paranoia

Beliefs of being punished by God  
 or possessed by the devil

## Severe paranoia

Tactile hallucinations

Keyworker:

Co-worker:

Present medication:

Carer contacts:

Triggers:

*Relapse drill*

*Step 1: stay calm – yoga or meditation*  
 Contact keyworker/services to go out  
 and discuss feelings (PF or partner)  
 Make time for yourself, use partner  
 and mum for support  
 Coping with thought/problems

*Step 2: Distraction techniques (PTO)*

Take \_\_ mg \_\_\_\_\_ from emergency supply  
 Daily contact with services, if necessary  
 (discuss feelings, reality-testing)  
 Contact doctor regarding recommencing  
 or increasing medication

*Step 3: Admission to hospital or respite care**Hours of contact:*

Mon–Fri (9.00–5.00)

Tel:

Sat–Sun (10.00–5.00)

Tel:

*Out-of-hours contact:*

The patient selects any cards describing early signs that they have experienced in the process of becoming unwell, and places them in order of onset.

The early signs thus retrieved and arranged in order of onset form the basis of the individual's relapse signature. Patients are then encouraged to personalise their signatures through the use of any idiosyncratic early warning signs not already mentioned and through personalised descriptions of symptoms identified from the card sort. Discussion of these exercises is then used to clarify possible triggers such as periods of stress and underlying difficulties preceding illness. Additional information, for example, at what point the individual feels that they lose insight, is also gained. Emphasis is placed on supporting the individual in understanding the meaning of these experiences within his or her own life context.

### *Development of a relapse drill*

Following the identification of the relapse signature, patients are supported in constructing a three-stage action plan known as a 'relapse drill'.

Staging is an essential feature of the relapse drill. It follows directly from the early warning signs, which are stratified into three levels, from those occurring earliest in the relapse signature to those occurring immediately prior to the psychotic relapse. In general, the earliest early warning signs in the relapse signature tend to be non-specific symptoms, with low power to predict psychotic relapse. Interventions with potential risks (e.g. increases in antipsychotic medication) are generally used after the relapse signature has clearly progressed towards potential psychotic relapse.

The drill is developed collaboratively and focuses on patient strengths, carers and service resources. Past coping strategies and therapeutic interventions that have been found to be helpful in preventing relapse are reviewed collaboratively with the individual and incorporated into the drill. Specific early warning signs may suggest new approaches to offer further protection against relapse. For example, anxiety, dysphoria and other affective changes may respond to techniques incorporating stress management. Similarly, patients suffering from low-level psychotic phenomena may benefit from techniques designed to challenge

**Box 2b. Relapse prevention sheet (contd)****Name:** PF**Date:***Coping with automatic thoughts***What is the thought? – write it down****What is the evidence?****Are there any other explanations/ways of viewing the thought? (evidence to disconfirm this – use others to support) e.g. 'burning up' or 'extremely anxious'***Distraction techniques***Count backwards from 100 in 13s****Concentrate on positive images – nature, greenery***Coping with problems/stressors***State problem – write it down****Write down all possible strategies****Pros and cons of each strategy****Select the best solution***Additional techniques:*

delusional and dysfunctional thinking drawn from the cognitive therapy literature.

At each stage, the relapse drill considers three areas for intervention.

**Pathway to support**

Patients and carers are provided with details of how to contact the mental health services 24 hours a day, including weekends.

**Service interventions**

These may include increased contact with the keyworker, anxiety/stress management, a negotiated temporary increase in medication, respite care, counselling, cognitive therapy and home treatment.

**Personal coping strategies**

These consist of successful coping strategies that have been applied in the past by the individual, or new ones that have been suggested in the recall of the relapse signature.

***Rehearsal and monitoring***

Having identified an individual's relapse signature and drill, the patient and relevant involved

carers are provided with their own copies of the relapse prevention sheet and monitoring is outlined as a shared responsibility between the individual, carers and mental health services. To enhance effective use, the relapse drill is rehearsed using personalised scenarios and role-plays concerning the patient's response if he or she should detect early warning signs. Hypothetical situations are used to discuss any difficulties that might arise (for example, denial or panic responses) and how to deal with these.

***Clarification of the relapse signature and relapse drill***

Clarifying the relapse signature and refining the relapse drill are other important areas of monitoring. Individuals are encouraged to replace existing coping strategies, forms of support and service interventions with more effective ones learned from ongoing therapy or experience. In this way, impending or actual relapse is used as a positive opportunity to refine the relapse signature and improve the relapse drill, thus increasing control over the illness.

**Case study**

The following case study illustrates the above process as it applies to a young woman struggling to accept a psychotic illness and the steps necessary to prevent relapse.

PF, a 45-year-old married mother of three, was referred to mental health services following a prolonged period of persecutory and guilty delusions. This had been preceded by a brief period of elevated mood with mood-congruent delusions. Although her symptoms responded well to haloperidol, she refused to take medication following recovery.

During the relapse prevention work, PF disclosed her fear of another psychotic relapse. She was able to identify early warning signs of psychosis, progressing from feelings of inadequacy and dysphoria (usually in the context of social stressors), through brief symptoms of elation, to the development of frank persecutory and guilty delusions.

The earliest stage of the relapse drill focused on PF's own coping strategies to deal with low mood, on obtaining early support, and, given the important role of stressors in the onset of her symptoms, on stress management. The second stage focused on strategies that she had previously found helpful in decreasing elation (e.g. listening to sad music, reducing activity and eating regular large meals) and on pharmacological interventions. Despite the benefits, PF was reluctant to take medication, but eventually agreed to recommence haloperidol should her sleep pattern deteriorate. The relapse drill was then

**Box 3. Early warning signs of psychotic relapse***Thinking/perception*

Thoughts are racing  
Senses seem sharper  
Thinking you have special powers  
Thinking that you can read other peoples minds  
Thinking that other people can read your mind  
Receiving personal messages from the TV or radio  
Having difficulty making decisions  
Experiencing strange sensations  
Preoccupied about 1 or 2 things  
Thinking you might be somebody else  
Seeing visions or things others cannot see  
Thinking people are talking about you  
Thinking people are against you  
Having more nightmare  
Having difficulty concentrating  
Thinking bizarre things  
Thinking you thoughts are controlled  
Hearing voices  
Thinking that a part of you has changed shape

*Feelings*

Feeling helpless or useless  
Feeling afraid of going crazy  
Feeling sad or low  
Feeling anxious and restless  
Feeling increasingly religious  
Feeling like you're being watched  
Feeling isolated  
Feeling tired or lacking energy  
Feeling confused or puzzled  
Feeling forgetful or far away  
Feeling in another world  
Feeling strong and powerful  
Feeling unable to cope with everyday tasks  
Feeling like you are being punished  
Feeling like you cannot trust other people  
Feeling irritable  
Feeling like you do not need sleep  
Feeling guilty

*Behaviours*

Difficulty sleeping  
Speech comes out jumbled filled with odd words  
Talking or smiling to yourself  
Acting suspiciously as if being watched  
Behaviour oddly for no reason  
Spending time alone  
Neglecting your appearance  
Acting like you are somebody else  
Not seeing people  
Not eating  
Not leaving the house  
Behaving like a child  
Refusing to do simple requests  
Drinking more  
Smoking more  
Movements are slow  
Unable to sit down for long  
Behaving aggressively

expanded to include a number of scenarios to rehearse her responses to stressful home situations, automatic thoughts of inability to cope, and the detection of dysphoria, elation or sleeplessness.

Approximately two months later, PF's partner contacted her keyworker to say that PF had not slept for two nights and was experiencing extreme anxiety and persecutory ideation. She had tried to implement a number of coping strategies but had not taken any medication. As a result of an emergency visit, PF agreed to recommence haloperidol to improve her sleep.

Although the development of psychotic symptoms had not been avoided, her self-management was fed back to PF positively and she was encouraged to review her signature and drill.

In collaboration with her keyworker, she made a number of changes to her drill, deciding to contact her keyworker earlier on an informal basis if at all concerned about her health. Her partner was also educated about the nature of her illness, her early warning signs and possible coping methods. PF received increased cognitive therapy on coping with

intrusive thoughts, problem-solving and anxiety management, and techniques from this therapy were incorporated into her relapse drill. She agreed to resume maintenance medication, and the point at which this should be increased was made objective. An emergency supply of additional haloperidol was also obtained from her doctor (see Boxes 2a,b for a copy of her revised relapse signature and drill).

Some months later, PF herself rang to request an urgent visit. She reported insomnia, anxiety, low-level ideas of reference and a weakly held belief that she might be the devil. She identified that these ideas had been precipitated by a fight with her partner and by a self-initiated reduction in her maintenance medication. She had successfully initiated stress management and distraction techniques and had enlisted social support from her sister. However, on the night before the visit she had felt increasingly anxious. As a result of the emergency visit, she was advised to recommence her previous dose of maintenance medication and to continue her stress management techniques and her symptoms quickly

resolved. The fact that she had successfully acted on the relapse drill and prevented the progression of her mild psychotic symptoms was seen as a success and the relapse signature and drill were again reviewed for potential areas that could be clarified or improved.

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## Common problems

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Our experience has shown that there may be a number of problems in conducting relapse prevention by this methodology.

### *Lack of 'insight'*

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It may still be possible to construct a relapse signature among individuals who are unable to conceptualise their past psychotic experiences as unreal. Such was the case with a 24-year-old man, who, following his psychotic episode continued to believe that during his illness his musical compositions had been stolen by a famous rock band. He was, nevertheless, able to construct a relapse signature identifying problems of increasing dysphoria and self-neglect leading up to the development of the delusion without conceding the belief itself to be delusional. On some occasions, individuals may themselves refuse involvement in relapse work but consent to involvement of their family.

Similarly, other patients may concede that their psychotic experiences are not real, but may attribute them to factors other than 'illness'. This is especially the case among individuals suffering from their first episode of psychosis, where denial of illness may serve the function of preserving self-esteem and should not be overzealously challenged. Individuals may still be able to identify early warning signs while attributing their problems to a multiplicity of causes other than illness – such as alcohol, interpersonal conflicts or spiritual experiences. Acceptable interventions might include increased support from family and services and, with the goal of normalising sleep or preventing re-hospitalisation, temporary increases in medication may also be accepted.

More difficult to solve is the problem of early loss of insight. In our clinical experience there is a subgroup of people who, while having 'past insight' (McGorry & McConville, 1999) and an ability to construct a relapse signature retrospectively, lose 'present insight' early in the relapse process. Although families may be involved in the relapse drill in this group, we have also employed prospective monitoring using a standardised measure of early warning signs (Birchwood *et al*, 1989). Completed fortnightly

by the patient and a family member, it has been used to help teach the individual to discriminate the changed perceptual, cognitive or affective processes that constitute the relapse signature.

### *'Sealing over'*

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A concept related to, but separate from, insight is that of recovery style. A recovery style characterised by 'integration' is one in which the individual is aware of the continuity of his or her mental activity before, during and after the psychotic experience, assumes responsibility for his or her psychotic productions, is curious about the experience and has flexible ideas about recovery (McGlashan *et al*, 1975). On the other hand, an individual who 'seals over' tends to isolate the psychotic experience, views it as alien and seeks to encapsulate it. Individuals whose recovery style is that of sealing over may find the 'early warning signs' approach, with its focus on the close examination of the illness, anxiety-provoking. For them, it may be necessary to temporarily suspend the process of constructing a relapse signature and to attend to the establishment of a secure therapeutic alliance with mental health services through working on shared goals such as vocational and social aspirations.

### *Lack of syndrome stability*

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Particularly in the early phases of psychotic illness, there is evidence of a considerable lack of diagnostic clarity and stability, which may be increased by factors such as comorbid substance misuse and the individual's psychological reaction to the illness (McGorry, 1994). Thus, a similar instability in the clinical presentation of the early warning signs of psychotic relapse may be expected. Fortunately, each relapse may be used to clarify the relapse signature and to refine the drill. However, there is an unavoidable paradox inherent in this work: increasing clarity of the relapse signature and, therefore, potential increased control of the process of relapse, only emerges with the additional information gained through each psychotic relapse. This may be resolved by considering such information as crucial to reducing the duration of relapse, since untreated psychotic symptoms are linked to speed of recovery and subsequent relapse (Drury *et al*, 1996b).

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## Relapse signature: promises

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Perry *et al* (1999) recently reported on a study showing a significant increase in time to first manic

relapse among a group of patients with bipolar affective disorder who were randomly allocated to receive training in the identification and management of their individualised early warning signs relative to those in the control condition. Significant beneficial effects on social and occupational functioning were also found. A trial is currently in progress evaluating a similar intervention among patients with schizophrenia.

However, even if the methodology proves not to be suitable for all people with schizophrenia, for many it offers the promise of a reduction in the negative biological and psychological consequences of psychotic relapse. Importantly, also, it offers an opportunity for the individual to explore and take control of his or her illness and to develop a positive ownership for its management.

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## Multiple choice questions

- 'Early warning signs' of schizophrenic relapse:
  - often begin with dysphoric symptoms
  - usually develop over many months
  - are more likely to predict actual relapse if both neuroleptic and low-level psychotic symptoms are included as signs
  - are rarely identified by patients themselves
  - show considerable variability between individuals.



2. Schizophrenic relapse:
- a can never be prevented by stress management techniques after the onset of 'early warning signs'
  - b can be successfully treated by five-times-a-week 'personal therapy' concentrating on early life experience
  - c may be accelerated by the patient's reaction to the early symptoms
  - d can generally be prevented by the use of intermittent medication alone targeted at early warning signs
  - e increases the risk of residual symptoms and social disability after each episode.
3. A relapse signature:
- a is a type of schizophrenic writing disorder
  - b can be completed without the patient if a relative takes part
  - c requires attendance at out-patients
  - d involves a card sort exercise to select suitable patients
  - e should be preceded by attempts to understand the patient's attitude to his or her illness.
4. Problems with relapse prevention are associated with:
- a poor insight
  - b a recovery style characterised by 'sealing over'
  - c older age
  - d single marital status
  - e variation in the presentation of early signs in different episodes.
5. A relapse drill:
- a involves therapeutic intervention appropriate to different stages of early warning signs
  - b requires rehearsal using role-playing
  - c incorporates the patient's own coping strategies
  - d usually uses increased medication as the earliest intervention
  - e needs to be memorised by the patient.

## MCQ answers

1	2	3	4	5
a T	a F	a F	a T	a T
b F	b F	b F	b T	b T
c T	c T	c F	c F	c T
d F	d F	d F	d F	d F
e T	e T	e T	e T	e F