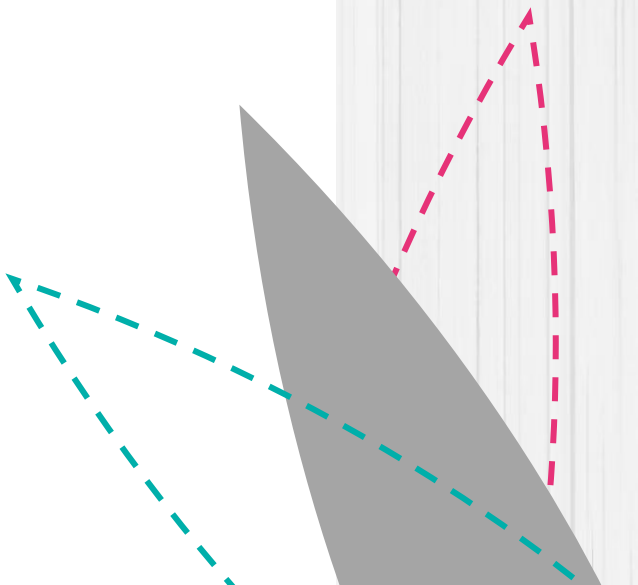
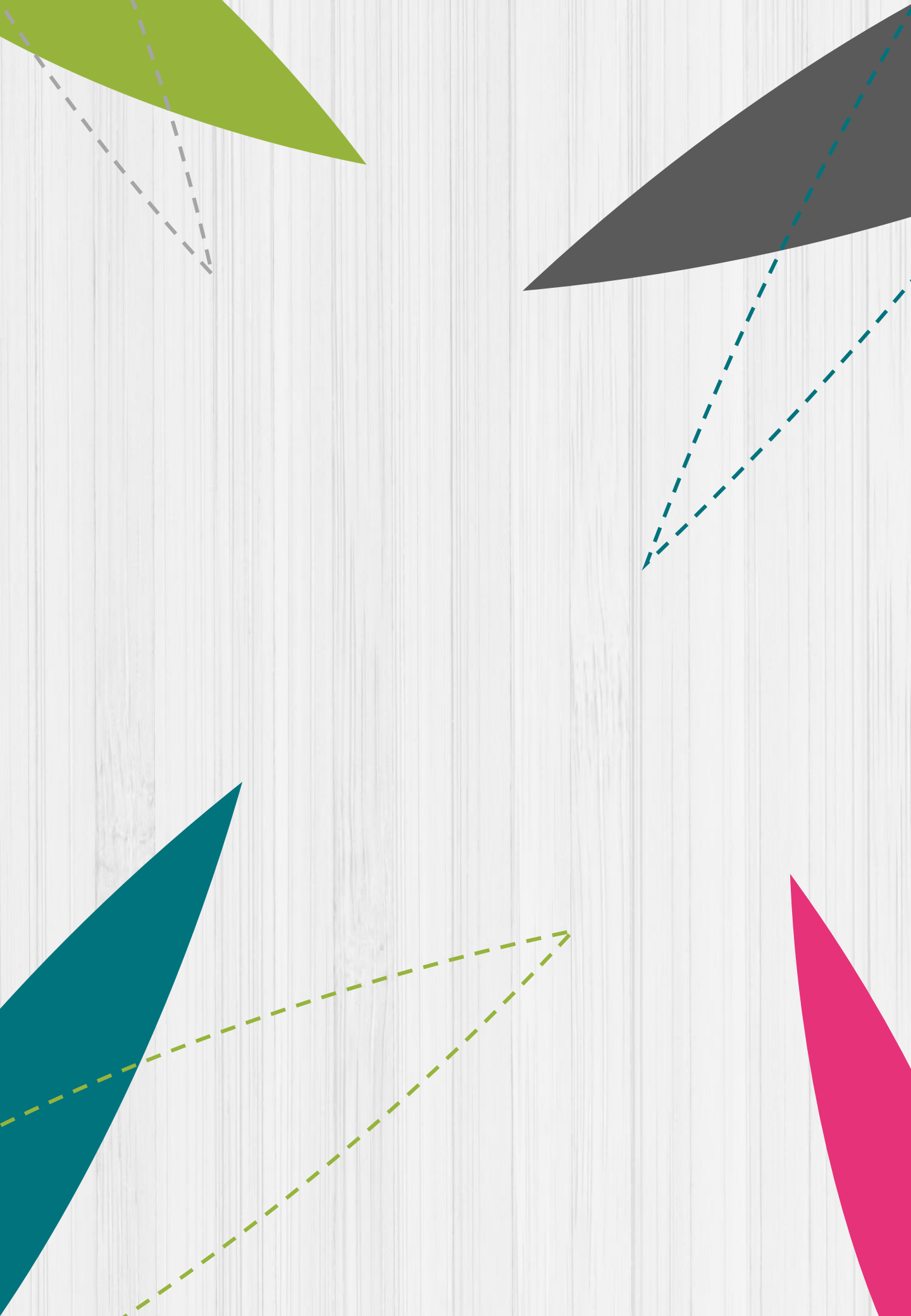
Understanding the Dimensions of Schizophrenia

White paper





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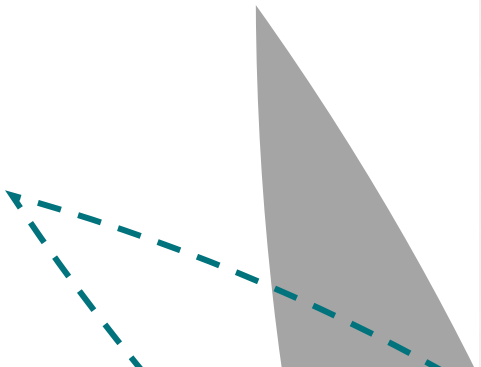
The symptom dimension of schizophrenia

Schizophrenia is a chronic psychiatric disorder affecting about 1% of the population worldwide. It was first described by Emil Kraepelin as a deteriorating psychotic disorder called '*dementia praecox*' that is characterized by cognitive impairment (1,2). Nonetheless, the term schizophrenia was first applied by Eugene Bleuler who argued that the symptom complex '*dementia praecox*' is not associated with dementia and emphasized how patients have a split psychic functioning (3). He also introduced the primary symptoms of schizophrenia such as abnormal associations, autistic behaviour and thinking, abnormal affect and ambivalence, laying out the basis of what we call schizophrenia today (3).

Almost a 100 years later since Kraepelin and Bleuler, the psychiatric community still aims to have a better understanding and description of this highly debilitating illness. According to the latest diagnostic manuals, the Diagnostic and Statistical Manual 5th Edition (DSM-5) and International Classification of Diseases 11th Revision (ICD-11), schizophrenia is characterized by positive symptoms such as hallucinations and delusions, negative symptoms, cognitive impairments, depressive symptoms, manic symptoms and abnormal psychomotor behaviour (4–7).

Importantly, the diagnosis of schizophrenia is still based on clinical observation of symptoms rather than biological markers such as genetic abnormalities, neurotransmitter dysregulations or anatomical alterations. Due to this, the conceptualisation of schizophrenia, especially the description of symptoms, is highly important.

Now, let's take a look at the core and forgotten symptoms of schizophrenia.



The core symptoms

The core symptoms of schizophrenia are undoubtedly the positive, negative, and cognitive symptoms. **Positive symptoms** refer to any change in behaviour or thoughts that is "extra" to normal, and they are the most known symptoms of schizophrenia. Positive symptoms are well managed by antipsychotic medications that act on the dopamine D2 receptors and therefore reduce or even eliminate false perceptions and bizarre beliefs (8).

POSITIVE

- Delusions
- Hallucinations
- Disorganized thinking
- Disorganized behaviour

NEGATIVE

- Anhedonia
- Blunted affect
- Alogia
- Asociality
- Avolition

COGNITIVE

- Deficits in speed of processing
- Attention problems
- Impaired judgement
- Problems with memory and learning

In contrast, **negative symptoms** describe "lacks" in different areas such as motivation or pleasure (9). Treatment of these symptoms is much more difficult, but not impossible. Research has also shown that the severity of negative symptoms play an important role in functioning and quality of life (10).

The third group, **cognitive symptoms**, encompasses all those symptoms that are related to cognitive functioning such as deficits in learning and memory, problems with concentration or impaired judgement. Functionality and independence is also highly related to the severity of cognitive symptoms, making it an important clinical target to address (11).

The forgotten symptoms

The so-called forgotten symptoms of schizophrenia are those symptoms that are not necessarily considered as primary symptoms, rather as secondary symptoms to the before mentioned core symptoms.

Affective symptoms, defined as dysregulation of mood such as depressive, anxiety and manic symptoms, belong to this category (12). These symptoms are also strongly related to cognitive and negative symptoms (12) and are also described as highly disturbing for patients; affective symptoms can increase the risk of suicide and diminish quality of life (13).

Hostility, irritability, and aggressive behaviour are often described in patients with schizophrenia and are found to be associated with higher severity of positive symptoms, lower adherence to pharmacological treatment, as well as increased drug or alcohol consumption (14). Although there is an increased risk of violence in this patient population compared to the general public, it is important to note that not all patients are violent. In fact, they are more likely to be victims of violence.

Similarly to affective symptoms, hostility also has a major negative impact on the quality of life and social functioning; it affects the families and caregivers too (15). Many antipsychotic medications were found to be effective in treating hostile behaviour, but adjunctive treatments are also common (16).

AFFECTIVE

- Depressed mood
- Suicidal ideation / attempts
- Anxiety
- Elevated mood

HOSTILITY

- Irritability
- Anger
- Resentment
- Aggression

The time dimension of schizophrenia

Besides symptoms, the other dimension to consider in schizophrenia is time, which addresses progression, and the stages over the course of the disorder.

Clinical staging is a well-described and -used concept in other areas of medicine such as cardiology or oncology, however it was introduced to psychiatry and schizophrenia only recently (17). The basic assumptions of clinical staging are that:

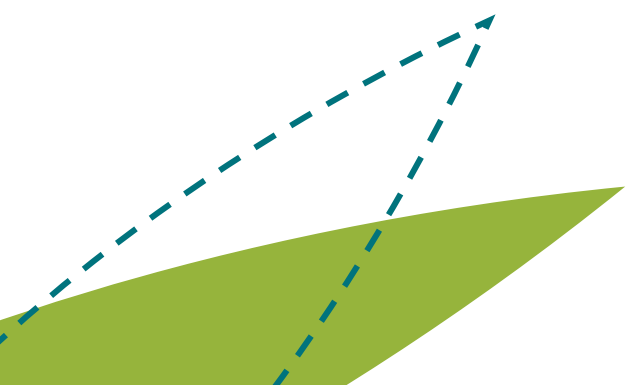
- treatment in the early stages of the disorder is more efficient,
- patients experience greater symptom severity in the later stages of the illness, and
- the progress of transferring to a later stage is connected with a typical clinical profile (18).

In case of schizophrenia, several staging models were developed in the past, however the most accepted and referenced is by McGorry and colleagues (19,20). According to their view, schizophrenia has 4 distinct stages: stage 0 increased risk, stage 1 mild and moderate symptoms, stage 2 first episode, and stage 3 persistent symptoms.

Recently, a systematic review merged the McGorry staging model and other models found in the literature into an integrated staging model, that resulted in the following stages:

- stage 0 prodrome,
- stage 1 acute manifestation of psychotic symptoms,
- stage 2 remission and relapse,
- stage 3 chronic schizophrenia.

So as a next step, after the review of symptoms, let's now focus on each stage in detail.



Stage 0. Prodrome

The 0th stage of schizophrenia is the prodrome, a period of the disorder when only mild or moderate symptoms are present, and a full-blown psychosis has not occurred yet (19). Due to the fact that this stage is preceding the first episode of schizophrenia, the prodrome is a retrospective concept that only be recognized afterwards (21,22). In terms of duration, the prodrome can last from weeks to years, but most typically, it lasts for about one year (21).

Throughout the prodrome, considerable changes affecting behaviour, thinking and mood can take place, and the patient can experience anxiety or even anger (23). The symptoms present during this time are heterogenous; mostly negative symptoms such as anhedonia, asociality or amotivation along with changes in perception, mood (anxiety, anger), beliefs and cognition (22,24).

Stage 1. Acute psychosis

The first stage is the onset of the first episode. Throughout this stage of schizophrenia, patients experience predominantly positive symptoms such as hallucinations or delusions and they might be in denial regarding their mental state (19,23). This denial may even manifest in hostile behaviour (25).

Currently, there is no strong scientific evidence regarding how long the first episode lasts or when it ends, nonetheless, it is estimated to cover the 2-5 years following first symptom occurrence (28–30).

The primary goal of treatment during this stage is to resolve positive symptoms and to facilitate recovery and return to normal life (31).

Stage 2. Remission & relapse

There are multiple scenarios how the disorder can continue after the first stage, hence this is the most heterogeneous part of the disorder.

According to the thumb rule described by Shepherd and colleagues, one third of the patients will go in remission and will not experience subsequent episodes (remission patients). The second third of the patients will experience one or more psychotic episodes (relapse patients); while the third group of patients will experience multiple relapses and unremitting illness which will be later described as chronic disorder (chronic patients) (30).

The primary treatment plan in this **stage** is relapse control and achieving remission. Remission is thereby defined as a period of the disorder when symptoms are mild and stable (31), whereas relapse is when symptoms start to reappear and the patient is experiencing a worsening in functioning (32,33).

Stage 3. Chronic schizophrenia

The **final stage** is chronic schizophrenia which is estimated to start 15-20 years after the first episode (28,34). Throughout this period the symptoms are still severe, persistent or unremitting (18). Patients might continue to experience numerous relapses while usually suffering mostly from negative, affective and cognitive symptoms, with the latter increasingly becoming the most prominent symptom domain of the disorder over time (18,34). Patients in this late stage are usually disabled and are likely to be unemployed or retired (28).

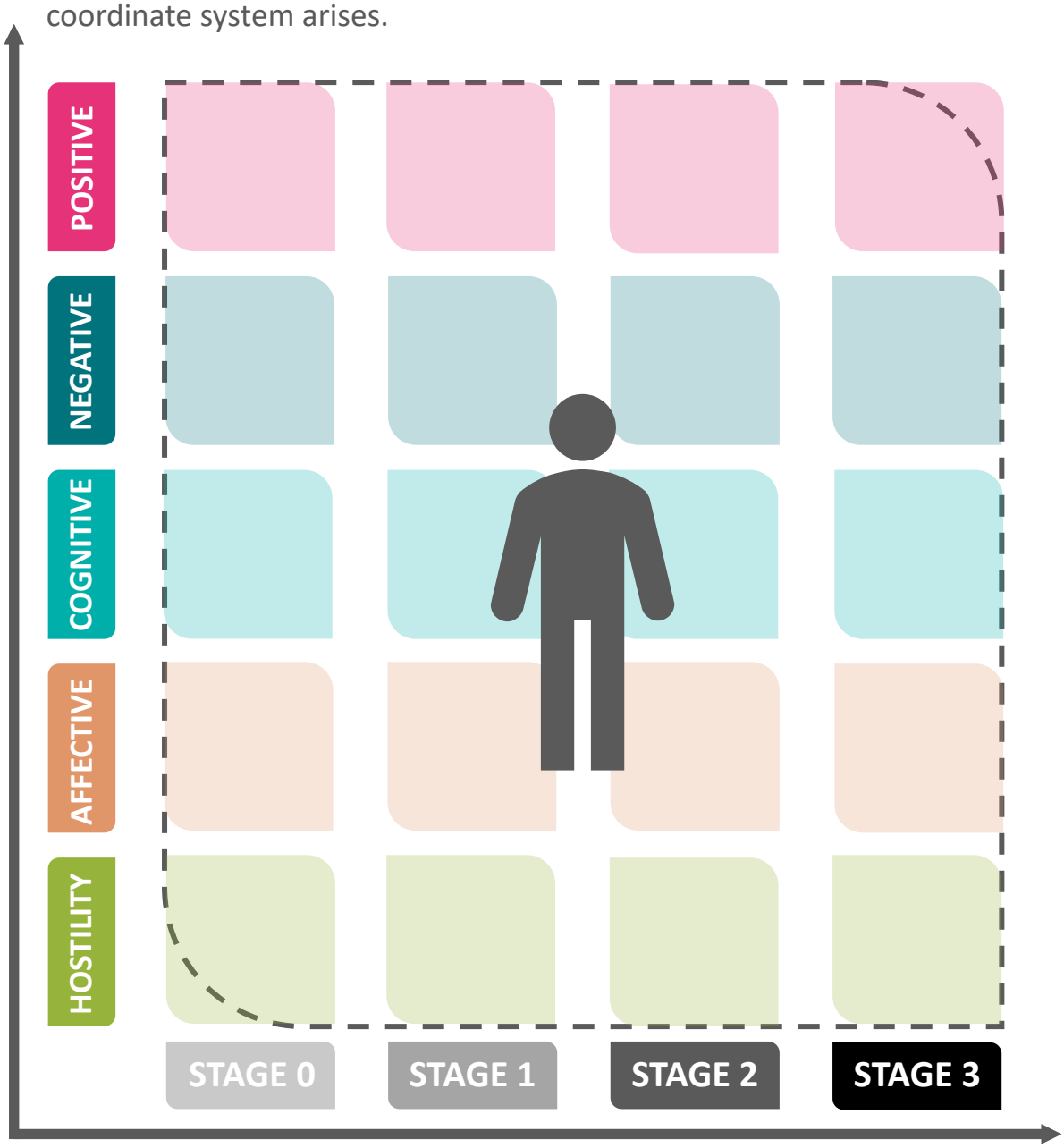
In the treatment plan of chronic schizophrenia there is a high emphasis on preventing of further exacerbation as well as long-term stabilization (19).

Patients within the dimensions of schizophrenia

Understanding the dimensions of schizophrenia in theory is just as important as recognizing where an actual patient stands within these dimensions.

One should aim to determine both the symptoms patients experience as well as at what stage of the disorder they might be currently at.

If putting symptoms on the Y axis and stages on the X axis, a clear coordinate system arises.

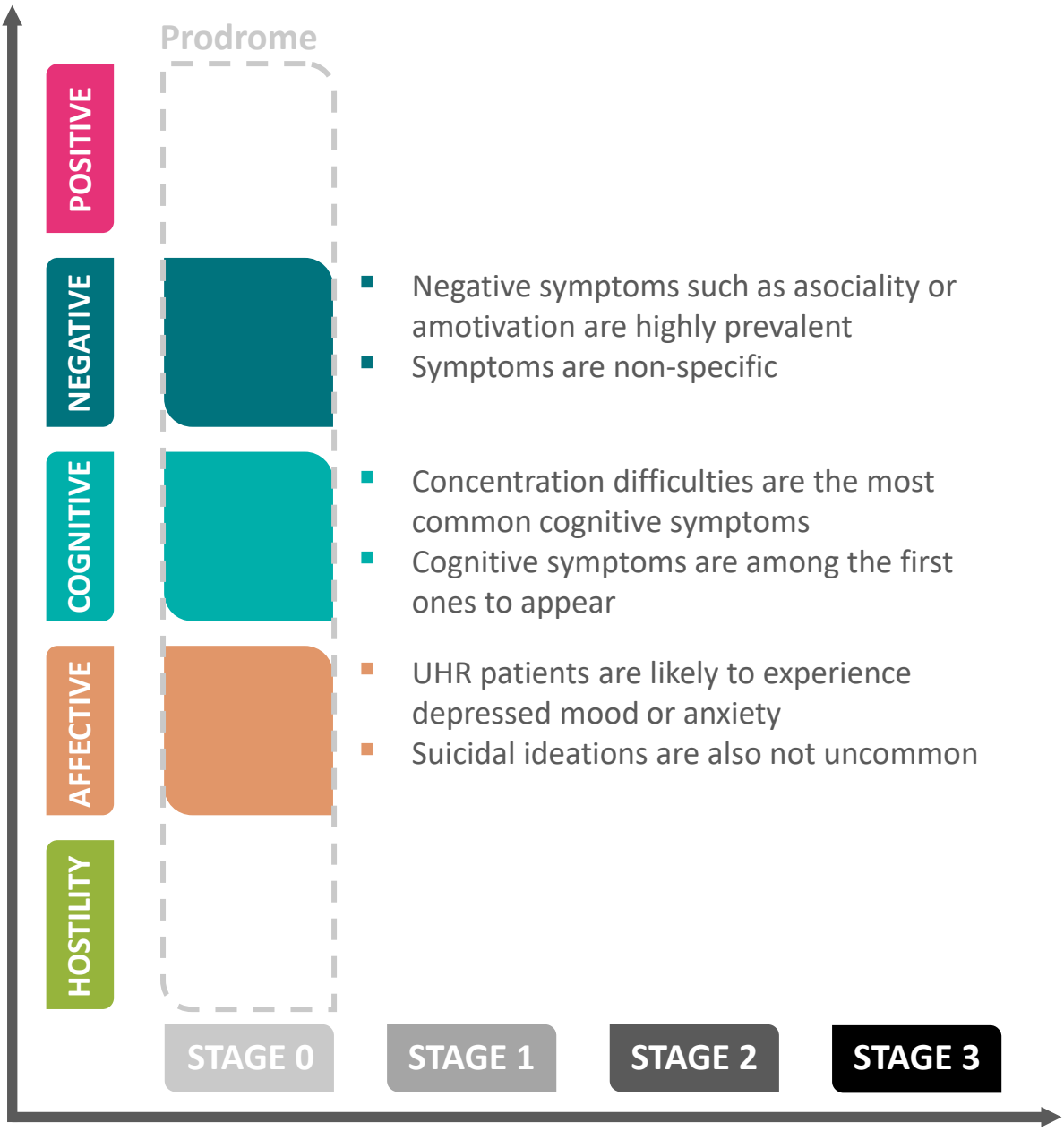


The ultra-high-risk patient

The ultra-high-risk patient (UHR) is at stage 0, prodrome. They experience predominantly negative and affective symptoms, as well as a certain level of cognitive impairment.

UHR patients cannot be diagnosed given that their symptoms are under threshold, nonetheless they still experience disturbances in their everyday life.

Given the lack of diagnosis, such patients usually receive psychotherapy without medication and pharmacotherapy is started once there is a definite diagnosis.



- Negative symptoms such as asociality or amotivation are highly prevalent
- Symptoms are non-specific

- Concentration difficulties are the most common cognitive symptoms
- Cognitive symptoms are among the first ones to appear

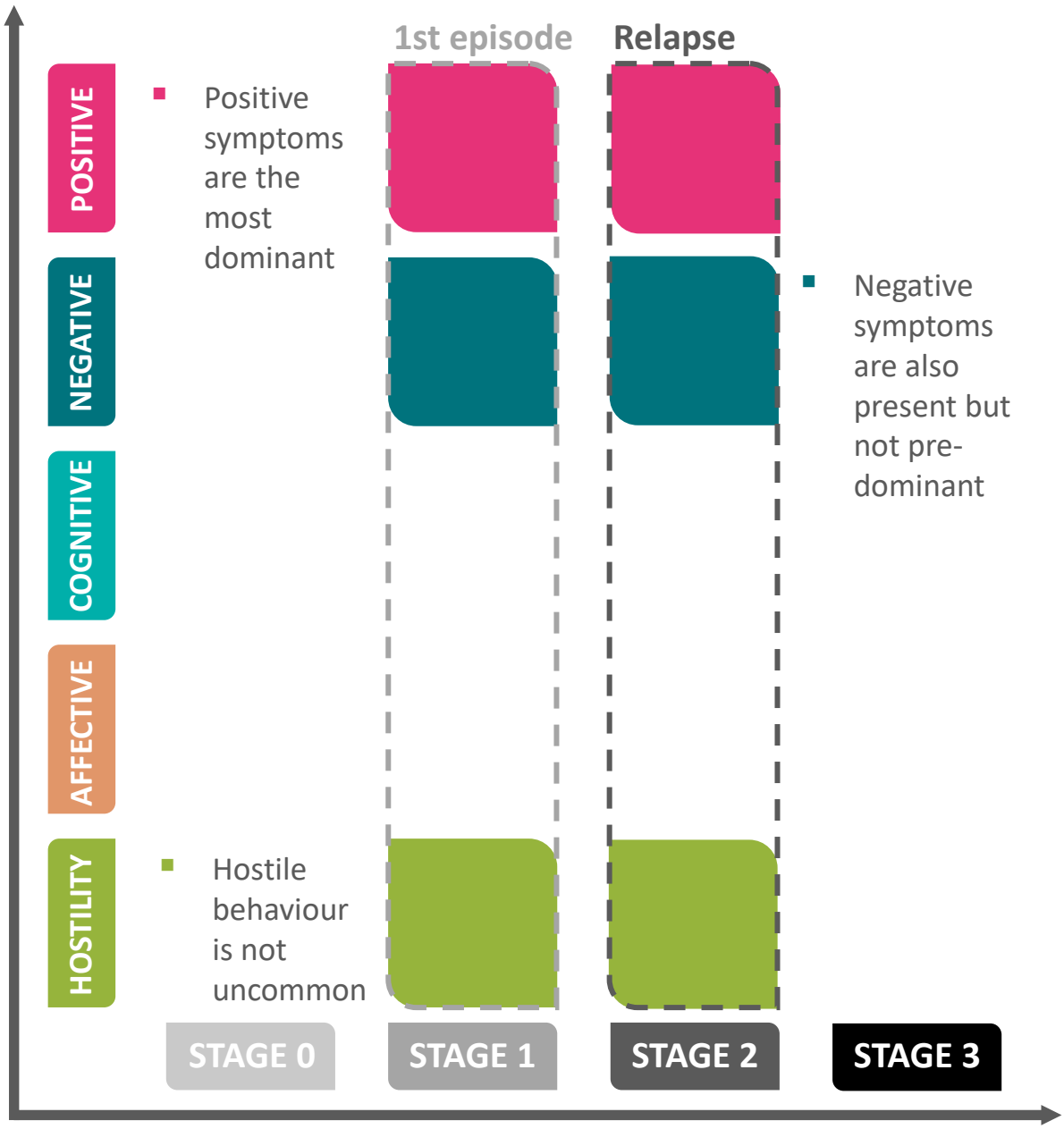
- UHR patients are likely to experience depressed mood or anxiety
- Suicidal ideations are also not uncommon

The acute patient

The acute patient can be either at stage 1, experiencing a first episode of schizophrenia, or at stage 2, experiencing a relapse in symptoms.

The most dominant symptoms in an acute patient are the positive ones such as hallucinations or delusions, but negative symptoms are also present.

Acute patients might be irritable or even aggressive, indicating the presence of hostility symptoms.

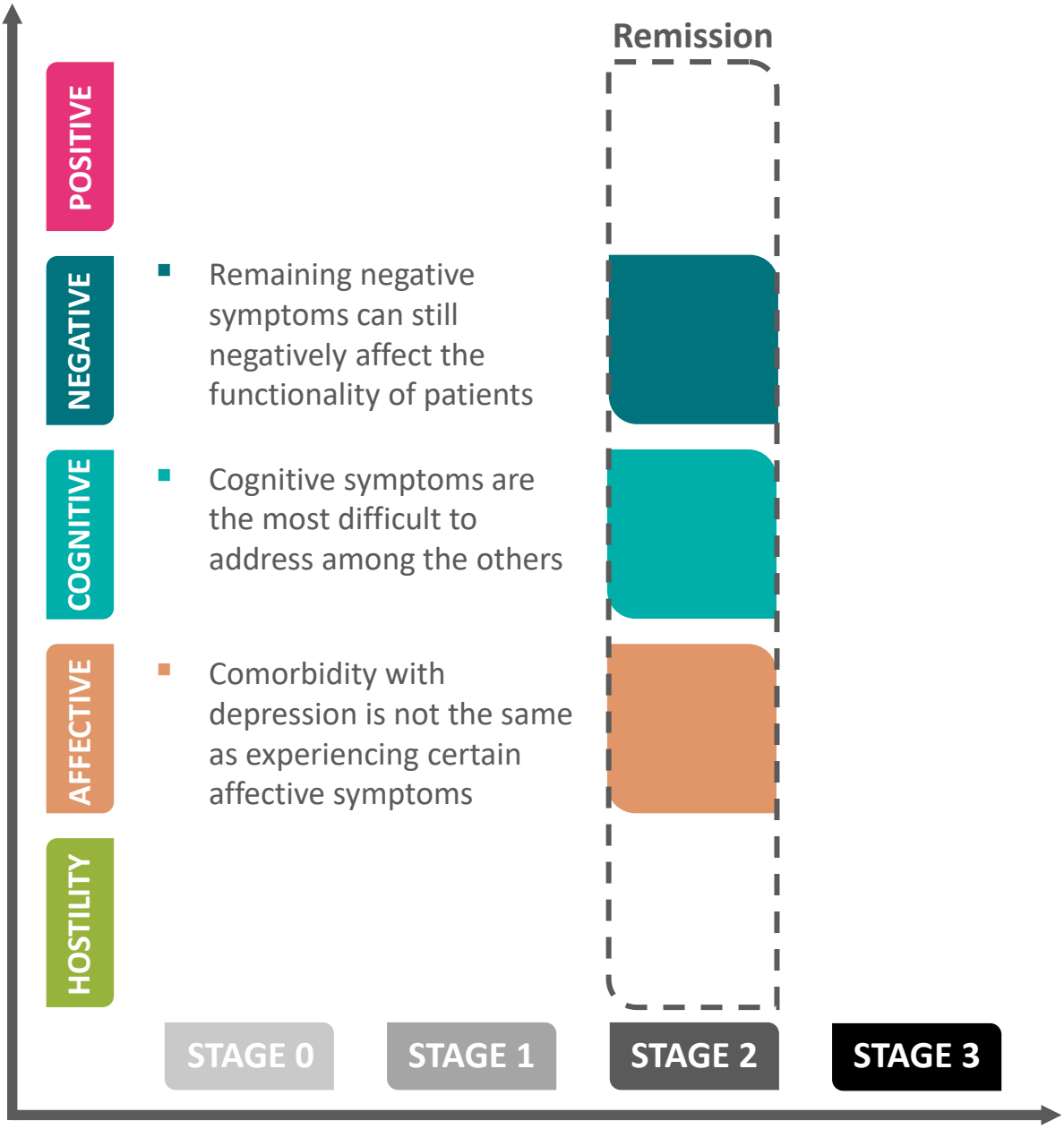


The remission patient

The remission patient is also in stage 2, however they experience a different mixture of symptoms compared to the acute patients.

Remission is not the same as recovery, therefore this patient group might still experience some mild or moderate symptoms that are negative, cognitive or affective in nature.

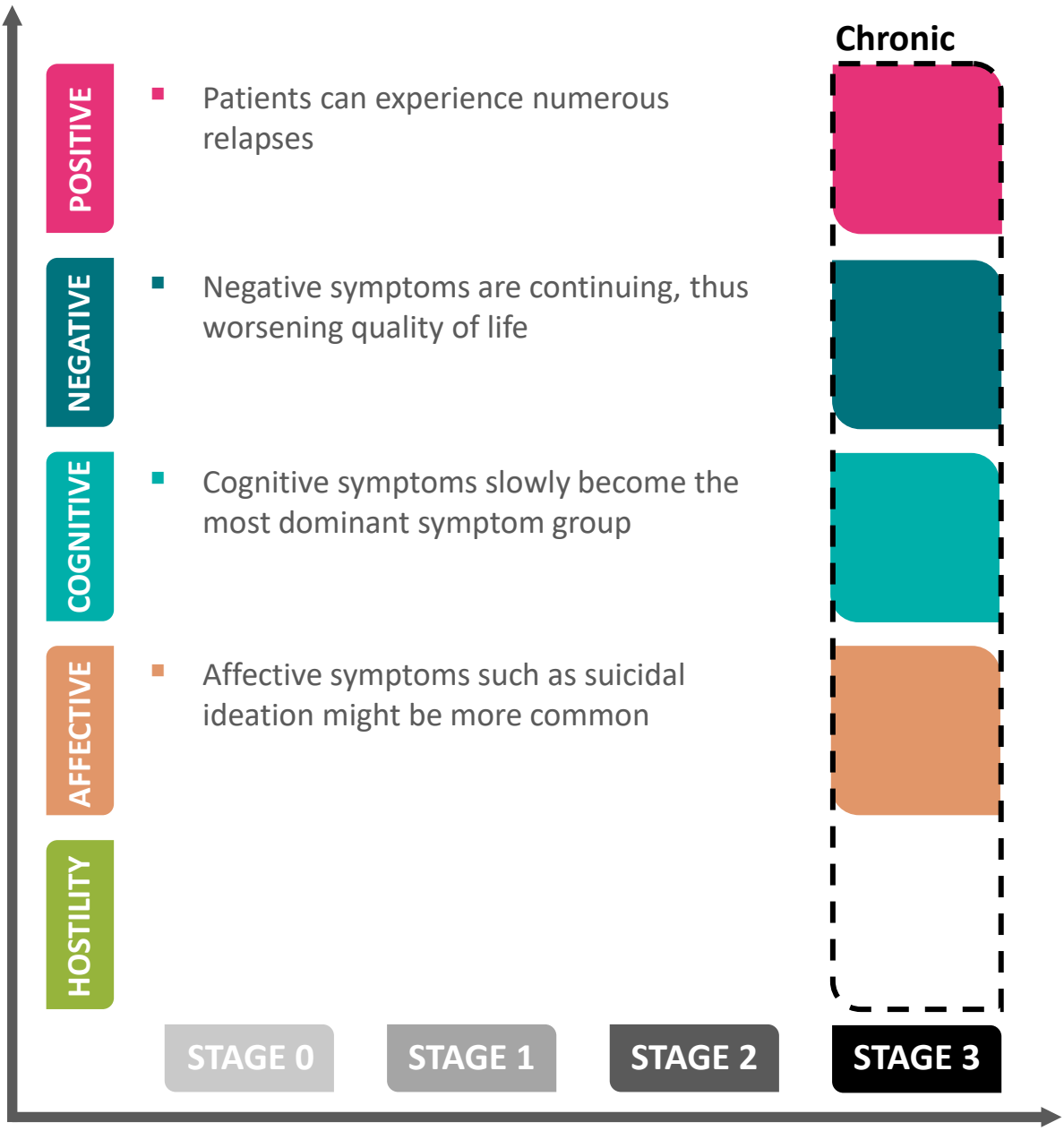
The main goal in these patients is to prevent relapse and further improve functionality and quality of life by reducing the remaining symptoms.



The chronic patient

Patients reaching stage 3 are the chronic schizophrenia patients. Although they are increasingly suffering from cognitive symptoms, they can also experience multiple relapses with underlying negative and affective symptoms.

The aim of treatment is to prevent patients from reaching this stage of the disorder, nonetheless it is not always possible. Hence, adequate pharmacological treatment and monitoring is crucial.



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