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## Psychological Characteristics and Treatment of Chronic Depression

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# 1

## General Introduction

### Introduction

Depression (also called Major Depressive Disorder (MDD)) is a state in which persistent depressed mood or loss of interest occurs together with other physical and mental signs, such as poor appetite, difficulties sleeping, impaired concentration, and feelings of hopelessness and worthlessness. A diagnosis of depression is only given when a number of these elements are present at the same time, for at least two weeks, and interfere with a person's ability to perform his or her day-to-day activities. The depression is called chronic when it is lasting two or more years, with less than a two-month period during which the individual reports no symptoms. Epidemiological and longitudinal studies show that approximately 20% of individuals with MDD in the general population and up to 47% of patients with MDD treated in primary and secondary care suffer from chronic forms of depression.<sup>1</sup>

In the first two editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM-I and II)<sup>2,3</sup> chronic depression was considered to be a personality disorder and therefore 'untreatable'.<sup>4</sup> This perspective began to change with the publication of DSM-III,<sup>5</sup> wherein dysthymia was introduced on Axis I as a chronic affective disorder. Chronic major depression emerged as a formal diagnostic category in 1987, when DSM-III-R<sup>6</sup> was published.

At the present time, the nosology of chronic depression differentiates among several chronic course subtypes: chronic major depression, double depression, recurrent major depression without full interepisode recovery, and chronic major depression superimposed on antecedent dysthymia.<sup>7</sup> The symptom criteria for dysthymia and chronic major depression overlap, but chronic depression requires a greater number of symptoms than dysthymia. Prospective research has shown that the majority of individuals with dysthymia eventually experience exacerbations meeting criteria for MDD at some point in their lives, which suggests that dysthymia and double depression may be different phases of the same disorder.<sup>1</sup>

In addition, few differences were observed between the various forms of chronic depression on a broad range of demographic, clinical, psychosocial, family history, and treatment response variables.<sup>8</sup> Therefore, it is suggested that chronic depression should be viewed as a single, broad condition that can assume a variety of clinical course configurations.

### Characteristics and risk factors of chronic depression

Compared to nonchronic forms of depression chronic depression is associated with greater disability, increased health service use, hospitalisation, higher likelihood of suicidal ideation and attempts, and higher burden of disease.<sup>1,9</sup> In addition, chronic depression

appears frequently in connection with psychiatric comorbidity, such as anxiety disorders, personality disorders and substance abuse, and somatic comorbidity, such as cardiac and respiratory syndromes, migraine, chronic fatigue syndrome, gastrointestinal ulcers, chronic bronchitis, arthritis, and back problems.<sup>9-12</sup>

Furthermore, there is some evidence that a history of childhood trauma, such as emotional neglect, psychological abuse, physical abuse and sexual abuse is associated with the development of chronic depression.<sup>13-16</sup> The role of childhood trauma in chronic depression is discussed in more detail in chapter 2. Finally, there is considerable evidence for the role of personality in chronic depression. Several studies have found that chronic depression was associated with higher levels of negative emotions (neuroticism) and lower levels of positive emotions (extraversion).<sup>17,18</sup> Neuroticism has also been found to predict a chronic course of depression.<sup>19-23</sup> Other psychological factors that appeared frequently in connection with chronic depression are: negative social interaction, feelings of inferiority, external locus of control, rumination and hopelessness.<sup>24,10,11</sup> The role of psychological factors in chronic depression is discussed in more detail in chapter 3.

The findings discussed above are mostly based on cross-sectional data. Only few longitudinal studies have investigated the development of chronic depression. Recently, a systematic review was conducted to examine which factors represent a risk factor for the development of chronic depression for patients diagnosed with MDD. Consistent results were found for the following factors: younger age of onset, the presence of a family history of mood disorders, and longer duration of the depressive episode.<sup>11</sup> However, as chronic depression is defined by the duration of the depressive episode, it can be questioned whether duration should be considered a risk factor for chronic depression. For clinical routine, the age of onset and the presence of a family history of mood disorders could be used as an indicator for a higher risk for a current depression to become chronic.

### Treatment of chronic depression

It is widely agreed upon that chronic depression is more difficult to treat than episodic major depression, and knowledge about optimal treatment approaches is emerging. Randomized, placebo-controlled trials have indicated that pharmacotherapy is efficacious in treating chronic depression.<sup>1,25</sup> A smaller, but growing, amount of randomized controlled trials have investigated the efficacy of psychotherapy for chronic depression.<sup>26</sup> In a meta-analysis of 17 studies it was found that psychotherapy had a small but significant effect ( $d=0.25$ ) on chronic depression when compared to control groups, however, it was less effective in comparison with pharmacotherapy ( $d=-0.31$ ). The combination of both psychotherapy and pharmacotherapy was found to be more effective in comparisons with pharmacotherapy alone ( $d=0.23$ ) and even more so in respect to psychotherapy alone ( $d=0.45$ ).<sup>27</sup>

However, relatively positive effects were found for the Cognitive Behavioral Analysis System of Psychotherapy (CBASP), a psychotherapy developed specifically to treat chronic depression. CBASP focuses on the pathological characteristics of chronically depressed patients, such as extreme interpersonal fear and avoidance and an external locus of control, which often stem from a developmental history filled with psychological insults and trauma.<sup>28</sup> In CBASP, beside the regular behavioral, cognitive and interpersonal techniques, specific techniques are used to replace the interpersonal fear of the chronic patient with interpersonal safety, starting within the therapeutic relationship. Subsequently, the relationship with the therapist is used as a tool to help patients to become more aware of their impact on others and to distinguish between adaptive and maladaptive relationships. Finally the avoidance strategies will be replaced with approach behaviors. The patient learns how to assert him or herself and how to interact in a functional way, creating a more internal locus of control.<sup>28,29</sup> The rationale and most important techniques used in CBASP are discussed in more detail in chapter 4.

In a large randomized trial (n=681) CBASP was compared to the antidepressant Nefazodone alone, and to their combination in chronically depressed patients.<sup>30</sup> After 12 weeks of treatment, CBASP alone was equally effective when compared to Nefazodone alone (48% response rate), while the combination of both treatments was clearly superior (73% response rate). Moreover, CBASP was also effective as a maintenance treatment for chronic depression<sup>31</sup> and was found to be a good alternative for patients who were not motivated for or refractory to pharmacotherapy.<sup>32</sup>

However, in a recent study, in which pharmacotherapy alone versus pharmacotherapy in combination with CBASP versus pharmacotherapy in combination with Brief Supported Psychotherapy (BSP) were compared in a group of chronically depressed patients (n=491) who had not achieved remission after 12 weeks of pharmacotherapy, it was found that the addition of psychotherapy (CBASP or BSP) did not produce significant differences in outcome compared to pharmacotherapy alone. Furthermore, the form of therapy specifically developed for chronic depression, CBASP was not more effective than BSP.<sup>33</sup>

Beside these mixed results obtained for CBASP, these results have been restricted to the assessment of efficacy. Both studies took place in academic settings, applied strict inclusion criteria, and participants were often recruited using advertisements in newspapers. Such situations do not reflect typical clinical settings, where most patients with chronic depression have been in treatment for years, suffer from severe symptoms, additional comorbid conditions, poor psychosocial functioning, and have a record of a poor response to previous treatments. Pragmatic applied research is therefore needed to evaluate the feasibility and effectiveness of CBASP for chronic depression in the real-world, outpatient settings.

In order to do so we conducted a multicenter randomized controlled trial in which we examined the effectiveness of CBASP for chronic depression in three specialized mental health care centers in the Netherlands. CBASP was compared to Care As Usual (CAU), which consisted of evidence-based treatments such as Cognitive Behavioral Therapy (CBT),<sup>34</sup> Interpersonal Psychotherapy (IPT),<sup>35</sup> and Short Psychoanalytic Supportive Psychotherapy (SPSP).<sup>36</sup> Pharmacotherapy was provided in both arms. It was hypothesized that CBASP would produce a greater reduction in depressive symptoms than CAU, since CBASP is specifically designed to treat chronic depression and has shown excellent results in the past.<sup>30</sup> The study protocol and results of this trial are discussed in chapter 5 and 6.

Finally, a relatively new and promising line of treatment for depression is Internet-based Computerized Cognitive Behavioral Therapy (CCBT). Several randomized controlled trials have confirmed the efficacy of clinician-guided CCBT for depression,<sup>37-43</sup> with effect sizes comparable to those associated with face to face treatment. However, little is known about CCBT and chronicity of depression. The increasing demands of managed health care to improve cost-effectiveness of treatment in combination with the likelihood that chronically depressed patients need longer periods of intervention suggest the utility of a form of therapy for chronic depression that can be self-administered, such as CCBT. Findings on chronicity of depression in patients treated Internet-based CCBT are discussed in chapter 7.

### Aims and outline of this thesis

Our aims were, first, to examine several potentially important characteristics of chronic depression, such as developmental (e.g. childhood life events, childhood trauma) and psychological (e.g. neuroticism, extraversion, locus of control) characteristics. Second, to investigate the effectiveness of CBASP, a psychotherapy that specifically focuses on these (pathological) developmental and psychological characteristics of chronically depressed patients. Finally, we wanted to explore whether a relatively new and promising line of treatment for depression, Internet-based Computerized Cognitive Behavioral Therapy (CCBT), can also be beneficial for patients with more chronic forms of depression.

Following our aims, in **chapter 2** the importance of childhood life events and childhood trauma for chronicity of depression is examined. **Chapter 3** contains the importance of psychological characteristics, such as neuroticism, extraversion and locus of control for chronicity of depression. **Chapter 4** covers the evidence, rationale and most important techniques used in CBASP. **Chapter 5** concerns the study protocol of the multisite randomized controlled that we conducted to test the effectiveness of CBASP in the Netherlands. In **chapter 6** the results of this trial are presented. To explore whether Internet-based Computerized Cognitive Behavioral Therapy (CCBT) can also be beneficial for patients

with more chronic forms of depression, we discuss the prevalence and predictive value of chronicity of depression in patients who have used Internet-based CCBT as a treatment for their depression in **chapter 7**. Finally, the results of chapter 2 through 7 are summarized, discussed and integrated with current knowledge in **chapter 8**.

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