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Recovery from Dysthymia and Panic Disorder

- Options and Obstacles

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“A ... serious obstacle to progress in psychiatry is difficulty of communication” –
Erwin Stengel, Bulletin of World Health Organisation, 1959

ABSTRACT

Dysthymia, a depressive disorder with usually an insidious, early onset (before age 21), and panic disorder are psychiatric disorders with a major impact on public health due to their high frequency of recurrence, persistent course and superimposed major depressions. This thesis aimed to improve knowledge of factors that help or hinder recovery from such disorders in ordinary outpatient psychiatric settings. A focus was how various understandings of illness may affect recognition, treatment and outcome. The thesis consists of a study that examined the validity of a self-report instrument for DSM-IV personality disorders, the DIP-Q, in different clinical samples (Paper I), and a prospective 9-year longitudinal study of patients with dysthymia and panic disorder that combined quantitative and qualitative methods (Papers II & III). Paper II presented the long-term outcome, stability of change and impact of comorbid personality disorders. For the investigation of lifetime course and treatments, a modification of the NIMH Life-Charting Methodology was used. Paper III examined the phenomenon of recovery by analysing in-depth interviews with qualitative content analysis. A theory-testing and explorative multiple-case study used developmental cognitive theory as a framework to examine barriers to recognition and treatment for patients with early-onset dysthymia (Paper IV).

Personality disorders (PD) evaluated by DIP-Q discriminated between different clinical samples and healthy controls, and the self-assessed PD had independent strong associations to depression and belonging to a sample of psychotherapy applicants. In Paper II, low recovery rates were observed; about 50% had improved, of whom 25% had recovered. Life-charting and case records indicated that undertreatment contributed to poor outcome. Comorbid PD was a negative prognostic factor and patients with panic disorder had deteriorated compared to the 2-year outcome. Based on the qualitative analysis in Paper III, a general model for recovery from dysthymia and panic disorder is suggested, involving: (1) understanding self and mechanisms of illness, (2) enhanced flexibility of thinking, (3) change from avoidance coping to approach coping, and that a helpful relationship to the health care provider is a vehicle for this change. Patients with dysthymia and panic disorder described specific helpful relationships to therapists ('as a parent' vs. 'as a coach') and central areas for change (self-acceptance and resolution of relational problems vs. identifying and handling feelings), indicating necessity of distinguishing early onset (before age 21) dysthymia from secondary depressions. The common main obstacle was difficulty in negotiating treatments. Non-remitted patients with PD had problems expressing needs, which may explain why comorbid PD is a negative prognostic factor. Paper IV showed that barriers to treatment of dysthymia could be explained by misunderstandings as patients mainly expressed illness with a complexity of concrete, perceptually bound language structures and providers focused mainly on a single aspect. Other barriers were patients' core pattern of concealing due to fear of rejection and distrust, providers' attitudes, access problems and providers' lack of follow-up.

To achieve higher recovery rates and reduce inequalities in attaining care, comorbid PD need to be assessed and addressed in ordinary psychiatric practice. Early-onset dysthymia needs to be recognised and distinguished from secondary depressions, e.g. by noting cognitive core symptoms and examining age of onset. To enhance collaboration, means of shared understanding and treatment planning are suggested, such as combining diagnostic assessments with attention to patients' perceptually bound understanding of illness, goals and treatment preferences, as well as systematic follow-up including re-evaluations. Life-charting may be a tool.

Key-words: dysthymic disorder, panic disorder, personality disorder, remission, recovery, mixed methods design, long-term follow-up, therapeutic relationship, patient preferences and experiences

LIST OF PUBLICATIONS

The thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

- I. Bodlund, O., Grann, M., Ottosson, H., & Svanborg, C. (1998). Validation of the self-report questionnaire DIP-Q in diagnosing DSM-IV personality disorders: A comparison of three psychiatric samples. *Acta Psychiatrica Scandinavica*, 97, 433-439.
- II. Svanborg, C., Åberg Wistedt, A. & Svanborg, P. Long-term outcome of patients with dysthymia and panic disorder: A naturalistic 9-year follow-up study. *Nordic Journal of Psychiatry. In Press 2008*
- III. Svanborg, C., Bäärnhielm, S., Åberg Wistedt, A. & Lützen, K. Helpful and hindering factors to remission in dysthymia and panic disorder at 9-year follow-up: A mixed methods study. *Manuscript*
- IV. Svanborg, C., Scarpinati Rosso, M., Lützen, K., Åberg Wistedt, A. & Bäärnhielm, S. Barriers in the help-seeking process: A multiple-case study of early-onset dysthymia in Sweden. *Nordic Journal of Psychiatry. Accepted Oct 2007*

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LIST OF ABBREVIATIONS

ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
APA	American Psychiatric Association
BZP	Benzodiazepine
BSI	Brief Symptom Inventory
DIP-Q	DSM-IV and ICD-10 Personality Questionnaire
DSM	Diagnostic and Statistical Manual of Mental Disorders
fMRI	Functional Magnetic Resonance Imaging
FU	Follow-up investigation
GAD	Generalised Anxiety Disorder
GAF	Global Assessment of Functioning
GSI	Global Severity Index
HAM-D	Hamilton Depression Rating Scale
ICD	International Classification of Diseases
ID-Scale	Impairment and Distress Scale
IIP	Inventory of Interpersonal Problems
LCM	Life Chart Methodology
NIMH	National Institute of Mental Health
MADRS-S	Montgomery-Asberg Depression Rating Scale-Self Assessment
OCD	Obsessive Compulsive Disorder
PD(s)	Personality Disorder(s)
PDA	Panic Disorder with Agoraphobia
PDWA	Panic Disorder Without Agoraphobia
PT	Post Treatment
SCID	Structured Clinical Interview for DSM
SCL-90	Symptom Checklist-90
SDM	Shared Decision Making
SSRI	Selective Serotonin Reuptake Inhibitor
TCA	Tricyclic Antidepressant
TR	Therapeutic relationship

INTRODUCTION

This thesis has been inspired by experiences as a psychiatrist and psychotherapist. The clinical practice can be frustrating as patients with depressive and anxiety disorders commonly have recurrences or a persistent course. Moreover, there is a growing awareness that the optimal outcome should be long-term remission and functional recovery, rather than short-term improvements of symptoms. This made me curious about factors affecting outcome for two diagnostic groups that are considered particularly difficult to treat – patients with dysthymia, and patients with panic disorder having agoraphobia. The simple questions were: Do any patients achieve enduring remission? What lessons can they teach us professionals? What are the obstacles to recovery in ordinary care? Comorbid personality disorder is a patient factor that is considered to worsen outcome and was therefore important to explore. In line with these questions, this thesis focused on psychiatric outpatients with long illness duration.

The perspective of health care providers and researchers is that knowledge of diagnostic categories guides recognition, treatment planning and investigations of psychiatric disorders. Furthermore, professionals tend to view the patient's suffering through the lens of their explanatory models, be these biological, social or psychological. From the patients' perspective, perceptions of illness are very complex and coloured by previous experiences, culture and social contexts. In treatment, these perspectives need to meet and reach consensus through communication.

Several assessment tools, mainly in the forms of structured interviews and self-report questionnaires, have been developed in order to help clinicians to distinguish diagnostic categories more reliably and to evaluate treatments. These instruments measure illness entities which the profession has defined at group level and they may overlook unique individual experiences. The connecting thought in this thesis is that clinical research which combines the perspectives of patients and professionals will give a more comprehensive picture of the phenomena under investigation. The epistemological framework is pragmatism, referring to "the theory that psychiatric explanations are 'true' only insofar as they promote beneficial real-world results for individuals with mental illnesses" (Brendel, 2003, p. 569). Major tenets of pragmatism are methodological pluralism, a patient-centred approach and that explanations must be useful and empirically testable in clinical settings (Tashakkori & Teddlie, 1998).

1 BACKGROUND

1.1 PREVALENCE AND SIGNIFICANCE

Anxiety and mood disorders tend to be chronic and recurrent. The burden of disability and suffering is significant, due to high prevalence, associated impairments, frequent early onset in childhood or adolescence and a substantial degree of persistence and comorbidity over the life-span (Wittchen & Jacobi, 2005). Half of all lifetime cases of mental disorder start by age 14 years and three-fourths by age 24 years. Later onsets are mostly of comorbid conditions (Kessler et al., 2005a). The prevalence of depression appears to be increasing, especially among children and adolescents, and age at onset is falling across generations (Hammen & Rudolph, 2003; Klerman & Weissman, 1989).

Dysthymia and panic disorder are two examples of diagnostic groups within this spectrum of non-psychotic mental disorders that have a major impact on public health. For example, in a European cross-country study, dysthymia and panic disorder were among the five mental disorders with the highest impact on work loss days, only second after neurological disease (Alonso et al., 2004). Another epidemiological study reported that serious impairment was found in 50 %, 45 %, and 30 %, respectively, of cases of dysthymia, panic disorder, and major depressive disorder (Kessler et al., 2005b). Among affective disorders, dysthymia has the strongest association to cardiovascular disorders (Baune et al., 2006). All mental disorders have an increased risk of premature death, with depressive disorders strongly related to suicidality (Bernal et al., 2007; Harris & Barraclough, 1998). The estimated 12-month prevalence is around 2 % for both dysthymia and panic disorder (Carlbring et al., 2002; Goodwin et al., 2005; Grant et al., 2005).

1.2 DSM CLASSIFICATIONS

Classification of mental disorders into diagnostic entities poses certain challenges, e.g. the difficulty of drawing a line between such disorders and normal reactions to strains in life, the paucity of physiological or radiological tests, complex value-laden aetiological assumptions, and problems of nosology. In a report to the World Health Organization 1959, the Austrian-British psychiatrist Erwin Stengel suggested that operational definitions would help to shape a common language for describing psychopathology (Stengel, 1959). A multi-axial, 'atheoretical', criterion-based system was introduced in the Diagnostic and Statistical Manual for Mental Disorders, 3rd Edition (DSM-III) (American Psychiatric Association, 1980). The system has gained widespread international acceptance, provided a basis for structured and semi-structured instruments for research and clinical practice, and stimulated an empirical basis for further revisions (Regier et al., 2002). However, the diagnostic categories in the DSM system are not completely discrete entities and there is a growing awareness of this categorical model's limitations (Widiger & Samuel, 2005).

1.2.1 Dysthymia and panic disorder

Dysthymia, defined as a depressive disorder with duration of at least two years, was introduced in DSM-III as a mood disorder, replacing the concepts of neurotic depression and depressive character disorder. Dysthymia has subsequently become a controversial diagnosis on account of its heterogeneity; there are problems in distinguishing it from major depression, personality disorders and depressions secondary to other psychiatric and somatic disorders. Panic disorder was delineated in

DSM-III from the former diagnoses of anxiety and phobic neuroses, describing recurrent panic attacks with associated fear of anxiety and sometimes avoidance of associated contexts (agoraphobia). Since then, panic disorder has been widely recognised and studied, resulting in effective short-term treatments.

1.2.2 Personality disorder

DSM-III introduced a multi-axial diagnostic system, assigning a separate Axis (Axis II) to personality disorders (PDs). This generated a psychiatric awareness of the diagnosis of personality disorder (PD) that was further stimulated by the adoption of operational criteria for diagnosing each PD, a procedure that was followed by ICD-10. The subsequent editions of DSM (DSM-III-R and DSM-IV) adopted polythetic categories for PDs. These categories are defined by a set of criteria, none of which are either necessary or sufficient for diagnosis. These rules lead to considerable heterogeneity in category membership because some members may have only few features in common. Moreover, cut-off scores may be set arbitrarily and create a false impression of a clear distinction between normality and pathology (Livesley, 2001).

To define clinical significance and maladaptivity, DSM-IV introduced the following general criteria for any personality disorder: (1) An enduring pattern of perceptions and behaviours with marked deviance in the sociocultural context, manifested in cognitions, affectivity, interpersonal relations or impulse control, (2) inflexible and pervasive patterns, (3) the pattern causes either significant functional impairment or subjective distress, (4) the pattern is stable and can be traced back to adolescence or early adult years, (5) not better explained by another psychiatric disorder, and (6) not caused by substances or somatic illness (American Psychiatric Association, 1994).

There are 10 specified personality disorders in the DSM-IV, arranged into three clusters: Cluster A; 'the Odd PDs' (paranoid, schizoid, schizotypal), Cluster B; 'the Dramatic PDs' (antisocial, borderline, histrionic, narcissistic), and Cluster C; 'the Anxious/Fearful PDs' (avoidant, dependent, obsessive-compulsive). Nearly three-quarters of patients diagnosed with a PD also present with a syndrome disorder. Although not being specific associations, Cluster A has been associated to proneness to psychosis, Cluster B to substance use disorders, and Cluster C to somatoform, anxiety and mood disorders (Dolan-Sewell et al., 2001).

1.2.3 Comorbidity

The delineation of diagnostic categories based on operational criteria has been important for communication within the psychiatric community, e.g. by enhancing reliability and accumulation of knowledge. However, the categorical diagnostic system is questioned due to overlap and boundary problems. Comorbidity among and between depressive disorders, anxiety disorders and PDs is the rule rather than the exception and is related to increased severity, longer duration and greater disability. About 30-40 % of individuals with anxiety disorders have a depressive disorder, and vice versa (Kessler et al., 2005b). In epidemiological studies, comorbid disorders can be present in up to 80 % of cases of panic disorder and up to 99 % of dysthymia, the latter on account of the extremely high correlation between dysthymia and major depression (Kessler et al., 2005b). The prevalence of comorbid PD is high (dysthymia 61 %, panic disorder with agoraphobia 76 %, panic disorder without agoraphobia 43 %) (Grant et al., 2005). Avoidant and dependent PDs are more strongly related than other PDs to mood and anxiety disorders. Associations with obsessive-compulsive PD are also significant (Grant et al., 2005).

Clark and Watson (1991) proposed a tripartite model to explain the high comorbidity of anxiety and depression. They suggested that the personality trait of

negative emotionality (or neuroticism) is the common structure and that the distinguishing structures are low positive emotionality (or anhedonia) in depression, and physiological hyperarousal in anxiety. They recently suggested a hierarchical model with two overarching factors – externalising and internalising (Clark & Watson, 2006). Substance-use disorders, attention-deficit and behavioural disorders, and antisocial personality disorder define the externalising factor. The internalising factor comprises two related factors: ‘distress/misery’ (comprising overanxious disorder, GAD, major depression and dysthymia), and ‘fear’ (comprising simple and social phobias, separation anxiety and panic disorder). A dimensional model has been suggested for personality disorders, comprising four dimensions: ‘neuroticism/negative emotionality/emotional dysregulation’, ‘extraversion/positive emotionality’, ‘dissocial/antagonistic behaviour’, and ‘inhibition/obsessiveness/persistence’ (Widiger & Simonsen, 2005). These hierarchical and dimensional models provide a framework for understanding comorbidity but do not give guidance for treatment planning and do not consider the evolution of disorders over time.

The extensive comorbidity between anxiety and mood disorders has led some investigators to question the relevance of differentiating dysthymia from anxiety disorders and to suggest the alternative concept of “cothymia”, a mixed anxious-depressive state combined with significant personality disorder of any type (Tyrer et al., 2003). However, among the two-thirds of patients with panic disorder who become depressed over their lifetime, some have primary, early-onset depression and others secondary depressions (Ballenger et al., 1998; Stein et al., 1990). This may be a confusing factor in research as well as in clinical practice.

1.3 REMISSION AND RECOVERY

Accruing experience has elucidated the importance of treating depression to full remission, as residual symptoms and functional impairments strongly increase the risk of relapse and recurrence (Judd et al., 1998; Kennedy et al., 2007; Paykel et al., 1995). One explanation for residual symptoms after resolution of an acute depressive episode is persistence of antecedent dysthymia (Keller & Boland, 1998). The evidence is less clear for anxiety disorders but it is reasonable to assume that treating to remission is equally important (Ballenger, 2001). The optimal outcome of treatment is cure, i.e. full recovery from illness. Recovery implies long-term remission of symptoms, resolution of functional impairments and the possibility of discontinuing treatment. Like many other medical conditions, depressive and anxiety disorders are to large extent chronic conditions, which imply that underlying vulnerabilities seldom are cured.

Guidelines and definitions for remission have been established for depressive and anxiety disorders (Ballenger, 1999; Gwirtsman et al., 1997; Keller, 2003). Definitions have mainly focused on symptomatic outcome (no or minimal symptoms) and diagnostic criteria. Additional criteria include no or minimal functional impairment and overall severity of illness. Some definitions for panic disorder include resolution of agoraphobic avoidance. The time criterion for remission varies between 2 weeks and 12 months; the most common definition of recovery is sustained remission for 6 months. However, the notion of recovery (or enduring remission) remains elusive because the meaning of the definition and the mechanisms of recovery are unclear, as are the mechanisms underlying the disorders.

1.4 GENERAL VIEW

The following sections present a review of the literature on dysthymia and panic disorder. The focus is on treatment and predictors of outcome. Further, boundary problems make it essential to elaborate the definitions, especially for dysthymia. However, the review does not cover the area of aetiological research. The general view of this thesis is that the origin of mental disorders can be comprehended in a biopsychosocial model (Engel, 1977). The model includes vulnerability factors of biological, psychological, and environmental origin, as well as stressors and cultural-societal factors that affect the expressions and conceptual models of illness. The focus of this thesis, however, is on healing and maintaining mechanisms. With that in mind, I have included a section on the therapeutic relationship. Moreover, a biopsychosocial model implies that both pharmacological and psychotherapeutic approaches to treatment are relevant.

1.5 DYSTHYMIA

1.5.1 Definitions and subgroups

The introduction of dysthymia in DSM-III was supported by prospective studies of neurotic depression by H. S. Akiskal and coworkers which demonstrated a recurrent unipolar or bipolar outcome in nearly 50 %; other patients followed a chronic or intermittent depressive course, or suffered from various anxiety and/or substance disorders (Akiskal et al., 1978). Akiskal proposed four subtypes: (1) Early onset 'subaffective' dysthymia, with depressive disorders in the family and responsiveness to antidepressant medication, (2) 'character-spectrum' disorder, with childhood adversities and comorbid personality disorders, (3) secondary dysthymia due to non-affective psychiatric or somatic disorders (sometimes labelled 'anxious dysthymia'), and (4) incomplete remission from late onset primary major depression (Akiskal et al., 1981; Akiskal et al., 1980).

In DSM-III-R (American Psychiatric Association, 1987), persisting depressive states following major depressive episodes were labelled chronic major depression and distinguished from dysthymia proper. DSM-IV has retained this distinction, but expelled the DSM-III-R distinction between primary and secondary dysthymia due to difficulties in the retrospective evaluation of primary diagnosis. In DSM-IV, dysthymia is defined as a depressed mood on a majority of days during at least two years, and at least two of the symptoms in Table 1. There should not be any period longer than 2 months without symptoms and no major depressive episode during the first two years of the disorder. For children and adolescents, the mood can also be irritability and the duration criterion is one year (American Psychiatric Association, 1994). Dysthymia is thus conceptualised as a subsyndromal yet more persistent form of major depressive disorder. However, the delineation towards chronic depression and depressive personality disorder is still an area of debate.

1.5.2 Course and alternative criteria

The current classification of unipolar depressive disorders is based on two dimensions: severity and course. The course specifiers were introduced in DSM-IV after a Mood Disorders Field Trial (Keller et al., 1995). The trial also evaluated the symptom criteria for dysthymia vs. major depression. In dysthymia, cognitive and social/motivational symptoms predominated, while vegetative and psychomotor symptoms were less common. A NIMH meeting achieved consensus on six core symptoms as typical of dysthymia, shown in Table 1 (Gwirtsman et al., 1997).

Table 1. Symptom Criteria for Dysthymia and Depressive Personality Disorder, Respectively

Current DSM-IV Dysthymia Symptom List	Consensus Essential Dysthymia Symptom Criteria	Provisional DSM-IV Depressive Personality Disorder Criteria
Dysphoric mood > 2 years	Dysphoric mood > 2 years	(1) Dejected, gloomy, cheerless, joyless
(1) Low self-esteem	(1) Low self-esteem	(2) Inadequate, worthless, low self-esteem
(2) Feelings of hopelessness	(2) Pessimism, hopelessness	(3) Pessimistic
(3) Low energy or fatigue	(3) Low energy, low initiative	(4) Critical, blaming, derogating to self
(4) Poor concentration or indecisiveness	(4) Concentration, thinking problems	(5) Brooding, given to worry
(5) Poor appetite or overeating	(5) Irritability, excessive anger	(6) Negativistic, critical, judgemental to others
(6) Insomnia or hypersomnia	(6) Social withdrawal	(7) Guilty, remorseful

1.5.3 Chronic depression

Dysthymia sometimes presents in a “pure” form but more frequently with a superimposed major depressive episode, referred to as “double depression” (Keller et al., 1983). The reported rate of superimposed major depression varies from 75 to 90 % (Keller et al., 1995; D. N. Klein et al., 2006). Conversely, approximately 25 % of patients presenting with major depression have an antecedent dysthymia (Kocsis, 2003).

In contrast to the important differences that have been found between chronic and episodic depression, studies have failed to find differences among depression’s chronic forms (J. P. McCullough, Jr. et al., 2003; J. P. McCullough, Jr. et al., 2000). Given these findings and the infrequency of dysthymia without superimposed major depression, it has been suggested that chronic depression should be viewed as a single, broad condition that can assume a variety of clinical course configurations (Angst et al., 2000). However, although a number of clinical and family studies suggest that there are few qualitative differences between dysthymia and major depression, there are some exceptions, mainly pertaining to age of onset.

1.5.4 The early-late distinction

The subgroup distinction of dysthymia between early (before age 21) and late (age 21 and later) onset was introduced in DSM-III-R and has been retained due to evidence suggesting that early onset characterises a more homogeneous group. The early-onset group has been more severe at follow-up, has more episodes of major depression and a higher family prevalence of affective disorders, as well as more disturbances in endocrine systems (D. N. Klein et al., 1988; Szadoczky et al., 1994). Patients with early-onset dysthymia and episodic major depression can be found in the same families; however, dysthymia is also somewhat distinct in that it aggregates specifically in families with dysthymia (D. N. Klein et al., 1995). The higher rates of, and stronger familial link to, personality disorders in dysthymia compared to episodic depression are mainly associated with early-onset dysthymia (Garyfallos et al., 1999; D. N. Klein et

al., 1995; Pepper et al., 1995). Early-onset dysthymic patients have been found to report more childhood abuse and poorer parenting than patients with episodic major depression (Lizardi et al., 1995). Furthermore, a 12-year prospective study of childhood-onset dysthymia showed that underlying dysthymia increased the risk of recurrence of major depressive episodes compared to episodic depression (Kovacs et al., 1994).

1.5.5 Depressive personality disorder

In DSM-III, dysthymia was included on Axis I as a mood disorder, and there was no category for chronic depression in the personality section (Axis II). However, in the DSM-IV Appendix there was a provisional set of criteria for depressive personality disorder (DPD) that comprised the general criterion for personality disorders with persistent and inflexible, maladaptive patterns and at least five of the symptoms listed in Table 1. Patients with early-onset dysthymia with no remission periods overlap considerably with the criteria for DPD. Investigations of the overlap have produced widely disparate findings, from 18 % (McDermut et al., 2003) to 95 % overlap (Bagby & Ryder, 1999). Much of the overlap is due to sharing of the two factors: low self-esteem and feelings of hopelessness (Ryder et al., 2006). It has been suggested that DPD traits should be included in the diagnostic system, as patients with DPD have less likelihood of remission than dysthymic patients who do not fulfil the criteria for DPD (Laptook et al., 2006; Markowitz et al., 2005b).

1.5.6 Comorbid conditions

Patients with early-onset dysthymia show high rates of comorbid personality disorders (about 60 %), mainly in cluster B (borderline, histrionic) and cluster C (avoidant, dependent, obsessive-compulsive), but also in cluster A (paranoid) (Pepper et al., 1995). Concerning personality traits, they have higher neuroticism and introversion scores, as well as more avoiding/denying behaviours compared to episodic depressives (Angst, 1998a). Anxiety disorders have been found in roughly half of dysthymic patients (Markowitz, 1995). Substance abuse is found in 11-45 %, but dysthymic disorder must be distinguished from substance-induced affective symptoms. Compared to the general population, dysthymia is overrepresented among patients in primary care, and also among patients with various medical and neurological conditions, pain syndromes, sleep disorders, chronic fatigue, hypothyroidism, and somatoform disorders (Howland, 1993).

1.5.7 Pharmacotherapy

In this overview of treatment studies, I have chosen to focus on early-onset dysthymia and include studies on “pure” dysthymia, double depression and chronic depression, as the delineation of these subcategories of chronic depression is difficult and changes over time.

Various antidepressant medications – tricyclic (TCA), selective serotonin reuptake inhibitors (SSRI), monoamine oxidase inhibitors (MAOI) and other drugs (sulpiride, amineptine, and ritanserin) – have been shown to be of similar efficacy for short-term treatment of pure dysthymia and double-depression (Lima & Moncrieff, 2000). The acute treatment response (typically defined as ≥ 50 % reduction of HAM-D) to antidepressant medication is 45-55 %, and full remission is 25-35 % (Kocsis, 2003). Treatment with SSRIs appears to lead to better compliance due to less side effects (Lima & Hotopf, 2003; Thase et al., 1996). Three studies have compared subsamples of patients diagnosed with chronic major or double depression and found comparable response rates for the two diagnostic groups using four different antidepressants (Keller

et al., 1998; Kocsis et al., 1996) (Keller et al., 2000). For non-responders, there is some support for the benefit of switching to another drug (Thase et al., 2002).

1.5.8 Psychotherapy

There are few trials on the psychotherapeutic treatment for dysthymia and chronic depression. Although long-term psychodynamic therapy is frequently prescribed for dysthymic patients and models are outlined, there are no studies on the short- or long-term outcomes (Arieti & Bemporad, 1980; Markowitz, 1994; SBU, 2004). Marital and family therapy have been tested for depression, but not specifically for chronic depression (Beach & Jones, 2002; Keitner et al., 2003). Compared to episodic depressions, chronic depression is more difficult to treat with standard cognitive behavioural therapy (CBT) (Sotsky et al., 1991; Thase et al., 1994). Different adaptations of CBT and interpersonal therapy (IPT) have been tested. A 12-week group CBT was less effective in reducing symptoms compared to sertraline (a SSRI), but seemed to attenuate functional changes (Ravindran et al., 1999). One 16-week study has shown equal efficacy of CBT and fluoxetine (a SSRI) (Dunner et al., 1996). A specifically designed interpersonal therapy for dysthymia (IPT-D; 10-18 sessions) was more effective than placebo but less effective than sertraline (Browne et al., 2002; Markowitz et al., 2005a). A 6-session psychological treatment, Problem-Solving Treatment for Primary Care (PST-PC), improved remission more than placebo but less than paroxetine (a SSRI) in an 11-week trial (Barrett et al., 2001).

1.5.9 Combined therapy

Given the suboptimal effect of antidepressant medications and established psychotherapies for the treatment of chronic depression, tailored treatment models are of interest. Cognitive-Behavioral Analysis Systems of Psychotherapy (CBASP) is a specific psychotherapy for treating chronic depression and dysthymia, developed since the '80s by J. P. McCullough (J. P. McCullough, 1984; J. P. McCullough, Jr., 2003). CBASP integrates cognitive-behavioural models with an interpersonal focus. In a trial involving nearly 700 patients with chronic depressions (42 % double depression), the efficacy of CBASP (16-20 sessions), nefazodone and their combination was compared (Keller et al., 2000). At the end of the 12-week acute study, the response among patients with combination treatment was better (about 75 %) than for the monotherapies (about 50 %). In the continuation phase, patients with combined therapy maintained significantly more partial or full remission (90 %) compared to nefazodone (80 %) and CBASP (82 %) (Kocsis et al., 2003). In a cross-over study, the alternative treatment appeared to be effective for non-responders to the initial treatment (Schatzberg et al., 2005). In the maintenance phase, nefazodone or monthly CBASP was effective for preventing relapse (Gelenberg et al., 2003; D. N. Klein et al., 2004). An analysis of the acute phase showed that among patients with a history of early childhood trauma, psychotherapy alone was superior to antidepressant mono-therapy and combined treatment was only marginally superior to psychotherapy alone (Nemeroff et al., 2003). Overall, combined therapy seems to have specific advantages for chronic depression compared to non-chronic depression (de Maat et al., 2007).

1.5.10 Long-term outcome

Dysthymia and double depression are by definition fluctuating, chronic conditions, which make longer periods essential for evaluation. A review of follow-up studies found three that had investigated the outcome after more than 10 years (Piccinelli & Wilkinson, 1994). Among patients with "endogenous-neurotic" depression, the average rate for sustained recovery was 24 % and for persistent depression 12 %. In a 25-year follow-up of one of these three cohorts, 12 % remained fully recovered (Brodaty et al.,

2001). A Swedish 10-year follow-up study of 83 patients admitted in the early '60s to the psychiatric department in Umea with "reactio neurotico-depressiva", found that during this interval two-thirds had relapsed and there were high rates of interpersonal conflicts, attempted suicides and unfavourable home conditions (d'Elia et al., 1974).

More recent long-term investigations of dysthymia include two prospective, naturalistic studies with better defined samples. A study of 97 adults with early-onset dysthymia and 45 adults with non-chronic major depressive disorder followed the course and outcome of these individuals up to 10 years (D. N. Klein et al., 2006). Patients with dysthymia had a protracted course, a high risk of recurrence (recovery rate 74 %; risk for recurrence 71 %), and exhibited greater depression at the 10-year point compared to patients with non-chronic depression. The Nottingham study of neurotic disorder has investigated the outcome of 210 patients with dysthymic, panic and generalised anxiety disorders (Tyrer et al., 2004). At the 12-year follow-up, only 30 % were judged to be recovered and initial diagnosis did not contribute to outcome. Predictors for worse outcome were baseline severity of depressive symptoms, personality disorder, and single marital status.

At present, the best validated approach for achieving sustained recovery from chronic depression is maintenance pharmacotherapy (Dunner, 2001). However, this approach is dependent on patients continuing their medication and problems with adherence are common. Addition of psychotherapy may improve compliance and target other areas of depressive illness (Pampallona et al., 2004). Some studies indicate that subsequent CBT or IPT after pharmacologic treatment may be effective in preventing recurrence of major depressive episodes (Fava et al., 2004; Frank et al., 2000; Hellerstein et al., 2001; Hollon et al., 2005; Paykel et al., 2005).

1.5.11 Predictors

The following factors have been associated with a higher risk of relapse and recurrence of a depressive episode: higher number of previous episodes, residual symptoms, early onset, psychiatric and medical comorbidity (including presence of dysthymia), negative self-perception, low self-efficacy, greater number of life stressors, abnormalities in neuroendocrine function, poorer medication adherence, and a history of childhood trauma (Arnou, 2004; Cyranowski et al., 2004; Gopinath et al., 2007). The influence of early adversities on depression is supported by both human and non-human primate studies, showing sensitized stress systems (Gilmer & McKinney, 2003; Nemeroff, 2004).

Factors that influence the outcome of short-term treatment in depression are therapeutic alliance, perfectionism, and high harm-avoidance or neuroticism (Abrams et al., 2004; Hellerstein et al., 2000; D. N. Klein et al., 2003; Mulder, 2002; Zuroff et al., 2000). Many controlled studies find no or relatively little influence of comorbid personality disorder on short-term outcome for major and chronic depressions (Kool et al., 2005; Mulder et al., 2003; Newton-Howes et al., 2006; Russell et al., 2003). Factors influencing the long-term course of early-onset dysthymia and chronic depression are marital status, illness duration, childhood adversities, family history of chronic depression, comorbid anxiety and personality disorders, chronic stress, socioeconomic disadvantages, and racial/ethnic minority status (Gilmer et al., 2005; Hayden & Klein, 2001; D. N. Klein et al., 2007; Mueller et al., 1996; Riso et al., 2002).

To conclude, there are few long-term studies of early-onset dysthymia. They show that the long-term outcome is poor, and that comorbid conditions, neuroendocrine abnormalities and childhood adversities are negative prognostic factors. However, the mechanisms for attaining and maintaining recovery are unknown, except that adherence to antidepressant treatment may be an important factor.

1.6 PANIC DISORDER

1.6.1 Definitions and subgroups

The concept of panic disorder has been elaborated since the 19th century, e.g. in the terms ‘irritable heart’ (Da Costa, 1871), ‘panic attacks in melancholia’ (Maudsley, 1879), and ‘anxiety neurosis’ (Freud, 1895). Donald Klein’s (1964) observations that an antidepressant medication (imipramine) had effect on panic states were important for the definitions of panic disorder and agoraphobia in DSM-III. In DSM-IV, *panic attack* is defined as a demarcated episode of intense fear or distress, where at least 4 of 13 symptoms (e.g. palpitations, sweating, choking, nausea, dizziness, fear of losing control, going crazy or dying) develop rapidly and reach a maximum within 10 minutes (American Psychiatric Association, 1994).

DSM-IV differentiates between: (1) panic attacks connected to other specific anxiety disorders (e.g. social phobia, specific phobia), (2) panic attacks as separate phenomena, (3) panic disorder without agoraphobia (PDWA), (4) panic disorder with agoraphobia (PDA), and (5) agoraphobia without panic disorder. *Agoraphobia* is defined as: (1) fear of being in places or situations that are difficult or embarrassing to depart from, or where help is not available, in the event of a panic attack or panic-related symptoms, (2) the situations are avoided or endured with significant distress or fear of panic-related symptoms, alternatively endured together with an accompanying person, and (3) not better explained by another mental disorder. *Panic disorder* is defined as both: (1) repeated, unexpected panic attacks, and (2) a duration of at least 1 month of either: (a) fear of new attacks, or (b) fear of consequences of attacks, (c) behaviour change due to attacks. It should not be better explained by substance-use, or other somatic or mental disorders.

1.6.2 Comorbid conditions

It has been suggested that panic disorder with and without agoraphobia, respectively, are essentially different disorders because they differ in the rates of comorbid conditions (Starcevic et al., 1992). Individuals with PDA have earlier age of onset, longer episodes, more severe disability, panic symptomatology, and Axis I and II comorbidity than those with PDWA (Grant et al., 2006; Kessler et al., 2006). The co-occurrence of mood disorders (bipolar, major depressive and dysthymic disorders), other anxiety disorders (GAD, social phobia, OCD) and substance abuse is high (Angst, 1998b; Brown & Barlow, 1992; Goodwin et al., 2002). Comorbid personality disorder, predominantly in Cluster C, is common in PDA (Brown & Barlow, 1992). Patients with PDA and PD are more likely to have comorbid dysthymia than those without this combination (Klass et al., 1989). There is significant comorbidity with many medical illnesses, such as cardio-vascular and chronic obstructive pulmonary diseases (Zaubler & Katon, 1996).

1.6.3 Treatments and short-term outcome

Panic disorder is the most investigated anxiety disorder with studies (typically during 8-12 weeks) demonstrating the efficacy of different treatment approaches, especially of pharmacological and cognitive behavioural therapies (CBT) (Gould et al., 1995; Mitte, 2005; SBU, 2005). The main outcome measures in the majority of studies have been rates of panic-free patients combined with global clinical impression. Different classes of drugs (SSRI, TCA and BZP) show similar efficacy. A meta-analysis from 1995 reports the following mean rates of panic-free patients: pill-placebo 35 %, waiting list 29 %, psychological placebo control 42 %, SSRI & TCA 58 %, BZP 61 %, and CBT 74 % (Gould et al., 1995). However, this is not the most comprehensive outcome measure of remission, as a low number of panic attacks can be determined by

avoidance. Some studies include measures of agoraphobic avoidance and functional impairments.

There are very few studies on the efficacy of psychodynamic psychotherapy for panic disorder. One study found that the addition of brief dynamic psychotherapy to treatment with TCA reduced relapse rates at follow-up (Wiborg & Dahl, 1996). A specific emotion-focused psychotherapy was shown to be no more efficient than placebo (Shear et al., 2001). Recently, a panic-focused psychodynamic psychotherapy has gained preliminary support in comparison to applied relaxation (Milrod et al., 2007).

Concerning combination treatment with antidepressants and CBT, there is no clear evidence from meta-analyses that this has advantages (Mitte, 2005) (Furukawa et al., 2006). After termination of the acute phase, the combined treatments have been more effective than pharmacotherapy alone and as effective as psychotherapy. However, there is some evidence that it may be worth switching treatment to either CBT or pharmacotherapy after the other treatment has not worked (Heldt et al., 2006; Hoffart et al., 1993; Kampman et al., 2002).

1.6.4 Long-term outcome

In a review of 16 follow-up studies up to the mid '90s, Roy-Byrne & Cowley (1994) stated that "while most patients improve, few are 'cured'." Another review stated that in the long-term, 45 % were unremitted, 24 % showed a pattern of remission-relapse and 31 % had stable remission (Katschnig & Amering, 1998). However, evaluations of long-term outcome have to consider the type of panic disorder and the population. Epidemiological studies suggest that up to 22 % of the general population experience at least one panic attack during their lifetime (Kessler et al., 2006). About one in five of these persons develop panic disorder, of whom one in four develop subsequent agoraphobia. Long-term follow-up (FU) investigations have been performed with populations who have received treatment in psychiatric settings or participated in treatment trials, i.e., they are selected groups.

The longest investigation is a 47-year FU of 125 patients from an anxiety disorders clinic in Spain (Rubio & Lopez-Ibor, 2007). The rate of full recovery was 5 %, 90 % were taking BZD, and panic attacks had to a large extent been replaced by agoraphobic avoidance and somatisation. A Swedish 15-year FU of 55 patients (71 % originally agoraphobic) who had participated in the Cross-National Collaborative Panic Study (a 8-week placebo-controlled study with alprazolam or imipramine) found that 31 % were panic-free (full recovery 18 %; still on medication 13 %), 55 % had recurrent panic attacks and 18 % fulfilled diagnostic criteria (Andersch & Hetta, 2003). An 11-year FU of 24 patients from the Austrian site of the Cross-National Collaborative Panic Study found that 33 % had achieved full remission (no panic attacks last year, no or minimal phobia and disability last month) (Swoboda et al., 2003). During the month before FU, 87.5 % had no panic attacks, and 54 % showed no or only mild avoidance. The Harvard/Brown Anxiety Disorders Research Program (HARP) has reported on a 12-year naturalistic, prospective study of patients with various anxiety disorders (Bruce et al., 2005). With the exception of patients with PDWA, a majority of subjects were still in their intake episodes at FU. The average proportion of the 12-year period that had been spent in illness episodes was 78 % and 41 % for subjects with PDA and PDWA, respectively.

Regarding the long-term effectiveness of CBT compared to medications for panic disorders, a review found only three studies that met strict methodological criteria (Nadiga et al., 2003). Two of them showed a modest protective effect of CBT and the conclusion was that more studies are needed.

1.6.5 Predictors

The factors that are most consistently related to poor long-term outcome of panic disorder are agoraphobic avoidance, duration of illness, and comorbid depressive, anxiety and personality disorders (Katschnig & Amering, 1998; Pollack & Smoller, 1995; Scheibe & Albus, 1996). Other factors related to poor long-term outcome are separation from parents during childhood by death or divorce, high interpersonal sensitivity, low social class, and unmarried status (Noyes et al., 1993). The findings concerning the influence of comorbid depressive and personality disorders are somewhat inconsistent in both short-term and long-term studies (Alnaes & Torgensen, 1999; Dreessen & Arntz, 1998; Massion et al., 2002; Mennin & Heimberg, 2000; O'Rourke et al., 1996; Slaap & den Boer, 2001). However, most studies find that these factors do contribute to poorer outcome.

To conclude, panic disorder has a variable course and agoraphobic avoidance is a strong negative prognostic factor. Many predictors for poor outcome are shared with dysthymia, although the influence of comorbid conditions is more equivocal. Lack of differentiation between early-onset dysthymia and secondary depressions may be a confounding factor. Besides maintenance antidepressant treatment, factors for maintaining remission are incompletely known.

1.7 THE THERAPEUTIC RELATIONSHIP

1.7.1 Definitions

In psychiatric care, the relationship between patient and provider is the vehicle through which diagnoses are made, treatment plans are negotiated and most interventions are delivered. From this perspective, a key component for promoting remission and recovery is the development of a collaborative relationship.

The relationship between patient and provider is extensively studied in psychotherapy research under a variety of terms, e.g. 'therapeutic relationship' and 'alliance' (McCabe & Priebe, 2004). It has been elaborated in psychoanalysis since the days of Freud, involving the components of reality-based collaboration and transference-influenced attachment to the therapist (Horvath & Bedi, 2002). Other theoretical frameworks for conceptualising alliance are role theory, social constructivism, systems theory and cognitive-behavioural models (Follette et al., 1996; Gilbert & Leahy, 2007; McCabe & Priebe, 2004).

Based on the work of Bordin (1994), research on alliance from the client's perspective and emerging clinical consensus, Horvath and Bedi (2002) have suggested a working definition of alliance in terms of the quality and strength of the collaborative relationship. The concept consists of two broad components: (1) the positive affective bond, such as mutual trust, liking, respect and caring, and (2) collaboration and consensus on the goals and tasks of therapy, involving a purposeful and responsible partnership.

1.7.2 Empirically supported elements

A number of instruments have been developed to measure alliance by patients, therapists and expert judges. Although they do not measure exactly the same construct, the scales have high intercorrelations and cover the two components of bond and collaboration (Horvath & Bedi, 2002; McCabe & Priebe, 2004). Alliance, measured with these scales, has consistently been associated with treatment outcome, with correlations from .22 to .26 (Horvath & Symonds, 1991; Martin et al., 2000). The importance of developing a strong alliance early in treatment is consistently supported (Horvath & Bedi, 2002). Early engagement via shared understanding, agreements on

goals and expectations for improvement enhance collaboration and lessen dropout (Tryon & Winograd, 2002). Another empirically supported general element of the therapeutic relationship is the therapist's empathy, consisting of elements like understanding the client's frame of reference, attunement, and communication skills (Bohart et al., 2002; Duan & Hill, 1996; Thwaites & Bennett-Levy, 2007). The majority of studies have found support for the role of patients' expectations in relation to outcome but findings regarding preferences are less uniform (Arnkoff et al., 2002). The link between patients' treatment expectations (assessed prior therapy) and outcome has been shown to be mediated by patients' contribution to alliance (Meyer et al., 2002). A reasonable explanation is that hope is both curative (placebo effect) and enhances commitment to treatment.

1.7.3 Common and specific factors

A long-standing issue has been the extent to which the effects of psychotherapy can be attributed to factors that are common to all psychotherapies (e.g. the therapeutic relationship, a healing setting, education and a treatment rationale) rather than to specific factors (Butler & Strupp, 1986; DeRubeis et al., 2005). Specific factors refer to techniques that are based on the therapist's theoretical orientation (e.g. relational interpretations, exposure, cognitive restructuring). Based on extensive reviews of outcome research from the '70s to the '90s, Lambert & Barley (2002) summarised the proportion of the improvement in psychotherapy patients as a function of extratherapeutic change (40 %), common factors (30 %), expectancy (15 %), and techniques (15 %). The extratherapeutic factors included various kinds of self-help and social support, and patient factors such as severity, complexity and chronicity of problems. The conclusion that common factors are more important for outcome has been challenged by the identification of efficacious and specific treatments for specific disorders (e.g. exposure and response prevention for obsessive compulsive disorder) (DeRubeis et al., 2005), internet-based treatments (Linton, 2007), the time-line problem (that alliance can be a result of outcome), and that common and specific factors may interact differently for different disorders and patients (Kazdin, 2005).

1.7.4 Therapeutic relationship in psychiatric settings

During the past decade there has been an increased interest in the role of the therapeutic relationship (TR) in psychiatric settings, and in other types of treatment than psychotherapy (Priebe & McCabe, 2006). In this context, the notion of therapeutic relationship involves terms such as 'engagement', 'medication compliance', 'adherence' and 'collaborative relationship' (Catty, 2004). TR has been shown to predict outcome, e.g. in pharmacologic treatment of depression, in-patient treatment of schizophrenia, and case management (Howegogo et al., 2003; Krupnick et al., 1996; Svensson & Hansson, 1999; Weiss et al., 1997). Adaptations to psychiatric settings are necessary, e.g. by developing suitable measurements of TR (McGuire-Snieckus et al., 2007; Weiss et al., 1997).

According to patients, the quality of TR appears to be the most crucial factor in psychiatric treatment (Bjoerkman et al., 1995; Glass & Arnkoff, 2000; Johansson & Eklund, 2003; Paulson et al., 1999). Concerning patients' satisfaction with care, quantitative self-report questionnaires seem to elicit more positive evaluations than qualitative methods (Svensson & Hansson, 2006). A recent Swedish thesis on TR in psychiatric settings indicated that 'being understood' by the therapist/staff is one of the most central aspects of good care (Johansson, 2006). Thus, congruence of patients' and providers' illness understandings may be vital for enhancing collaboration and outcome. Moreover, incorporating patients' views on treatment and outcome may disclose novel aspects of helpful and hindering factors.

2 AIMS

The overall aim of this thesis was to improve knowledge of factors that help or hinder long-term remission of patients with dysthymia and panic disorder in ordinary psychiatric care. A focus was how patients' and providers' various understandings of illness affect recognition, treatment and outcome.

The specific aims were to examine:

- The validity of diagnosing personality by means of self-assessment with the DSM-IV and ICD-10 Personality Questionnaire (DIP-Q) in three clinical samples and healthy controls in relation to clinical and demographic factors (Paper I).
- Outcome and to compare stability of change at 9-year follow-up compared to 2-year outcome and the impact of comorbid personality disorder in a naturalistic treatment study of patients with dysthymia and panic disorder (Paper II).
- The phenomenon of remission by investigating the perceptions of patients with dysthymia and panic disorder with different long-term outcomes at 9-year follow-up, by exploring: (a) perceived helpful and hindering factors, (b) common and specific factors, and (c) convergence of patients' subjective views on remission with diagnostic assessments (Paper III).
- Barriers to diagnosis and adequate treatment of patients with early-onset dysthymia by studying how the patients' and providers' understandings of illness have evolved and how treatments have been negotiated over time (Paper IV).

3 MATERIAL AND METHODS

3.1 QUANTITATIVE, QUALITATIVE AND MIXED METHODS

3.1.1 Choice of method

With the aim of improving knowledge of helpful and hindering factors in long-term remission in ordinary psychiatric care, a longitudinal, naturalistic study of patients with long illness duration was performed (Papers II-III). The rationale for a concurrent mixed design (combining quantitative and qualitative methods) was based on the assumption that professionals and patients have different insights into psychiatric illness and recovery, and that triangulation of perspectives and methods would give a more comprehensive understanding of these phenomena. Participants were selected from several clinical populations in order to cover different clinical settings, since contexts can affect assessment, process and outcome. The findings in Papers II-III led to the formulation of research question for Paper IV. The complex and context-bound purpose influenced the choice of a multiple-case research design for this paper.

Psychiatric research needs to define and measure clinically relevant subjective conditions and experiences of individuals and groups of patients. Methods have been developed to facilitate standardised evaluations of diagnosis and outcome, comprising expert ratings and patients' self-reports. We need to be aware of the strengths and limitations of these instruments (Paper I). In using them we seek to quantify illness entities that have been defined at group level by professionals but may overlook relevant experiences at the level of the individual.

Patient-centred research endeavours to understand the illness experience from the standpoint of the individual, i.e. sees the patient as the expert on subjective aspects of her/his illness. This line of research has, on the other hand, been accused of naively accepting the informants' descriptions and being biased by preconceptions. In this thesis, the attitude to these issues is that preconceptions, previous experiences and theoretical frameworks always influence the research process. My background as a clinician and cognitive-behavioural therapist has influenced the choice of research questions and methods, as well as the interpretation of data. However, the research procedure should assure that the findings are grounded in the data rather than in preconceptions. Qualitative methods may help to bridge the gaps between research and clinical practice, and it has been suggested that "by combining qualitative and quantitative approaches, the shortcomings of both strategies can be offset" (Malterud, 2001, p. 399). As the mixed-methods approach is not standard in psychiatric research, a tentative outline of some definitions and core issues is given below.

3.1.2 Research approaches

Paradigms, according to the writings of T. Kuhn, may be defined as both epistemological stances and shared belief systems that guide researchers (Kuhn, 1962, 1970). During the last 50 years, the predominant scientific paradigm in psychiatry and academic psychology has been positivism; science concerns measurable observations of phenomena and propositions that define relations between these phenomena. This epistemological stance is the basis for quantitative research, experimental designs and the hypothetic-deductive method. Qualitative research, based on constructivism, naturalistic inquiry and a holistic-inductive view of knowledge, has been used predominantly in the social and caring sciences. Constructivism is founded on the premise that humans interpret and construct reality, and that these constructions differ from the physical world and therefore must be studied differently (Patton, 2002b).

During the past decade, “mixed methods research design” has emerged as a separate research approach (Tashakkori & Teddlie, 2003). It has been defined as “the type of research in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inferences techniques) for the broad purposes of breadth and depth of understanding and corroboration.” (Johnson et al., 2007, p. 123).

The epistemological school connected with mixed methods is pragmatism, which originated from American scholars such as C. S. Peirce (1839-1914), William James (1842-1910), and John Dewey (1859-1952), and more contemporary theorists such as W. V. O. Quine (1908-2000) and Hilary Putnam (1926-) (Tashakkori & Teddlie, 2003). Pragmatists consider truth to be “what works” and claim that different theoretical perspectives and methods are both compatible and mutually informative. They embrace that both objective and subjective views are valid. In mixed methods research, quantitative as well as qualitative methods are used. Based on the writings of prominent advocates of the mixed methods approach, I have made a scheme that compares core issues in these three major approaches (Creswell, 2003; Morgan, 2007; Patton, 2002c; Tashakkori & Teddlie, 1998, 2003; Teddlie & Yu, 2007).

Table 2. Outline of Core Issues in Three Major Research Approaches

Core issues	Quantitative approach	Qualitative approach	Mixed methods approach
Epistemology	Positivism	Constructivism	Pragmatism
Relation: theory-data	Deduction	Induction	Abduction
Research process	Objectivity	Subjectivity	Inter-subjectivity
Inference	Generalisability	Context	Transferability
Sampling	Random	Purposeful	Both random & purposeful
Rationale for selection	Representative	Information-rich cases	Both representative & information-rich cases
Sample size	Large (>50)	Small (<30)	Multiple samples
Time for sample selection	Before	Before & during	Before (some during)
Selection procedure	Statistics	Expert judgement	Expert judgement
Depth/breadth	Breadth	Depth	Both depth & breadth
Type of data	Numeric	Narrative	Both numeric & narrative

Table 2 should be viewed as describing prototypical paradigms, because these features (or in the words of the pragmatists – these “lines of action”) are not truly separated in the ‘real world’ of research practice. Normally the empirical scientist moves back and forth between data-driven inductive analyses to theory-derived deductive analyses, although the approaches stress these analytic lines differently. The notion of *abduction* describes a combination of the deductive and inductive models (Patton, 2002a).

The tenet of positivism – that the researcher can be completely objective – has to a large extent been replaced by postpositivism, i.e. that research is influenced by the theories and values of the researcher (Tashakkori & Teddlie, 2003). One example of researcher bias is the allegiance effect, i.e., the tendency of investigators to obtain better results with the therapy modality they have a primary allegiance to or a financial interest in (Gaudiano & Herbert, 2005). *Intersubjectivity* is the pragmatic

stance that “has no problem with asserting that there is a single ‘real world’ and that all individuals have their own unique interpretations of that world” (Morgan, 2007, p. 72). This implies that it is important both to articulate and embrace subjectivity and to control it by consensus processes. Common strategies for handling the subjectivity of the researcher in postpositivist qualitative research are the use of external auditors or frequency tallies. In constructivist qualitative research, ‘bracketing’, ‘monitoring of self’ and ‘reflexivity’ are standard strategies (Morrow, 2005). In short, this means that the researchers seek to make implicit assumptions and biases overt to themselves and others, to carefully ground the analyses in the data, use self-reflective journals and a research team. *Transferability* refers to whether the findings in one context can be transferred to other settings. The pragmatic stance is that this is an empirical question.

The difference between the quantitative and the qualitative approaches also affects sampling methods, type of data gathered, analysis and how results can be used. Qualitative research is *idiographic* and *emic* (focusing on a few individuals, finding categories of meaning). In contrast, quantitative research is *nomothetic* and *etic* (focusing on large samples that are representative of larger populations, counting categories operationalised by the researcher) (Morrow, 2005). The logic in qualitative research is to select information-rich participants, i.e. *purposeful sampling* (Patton, 2002c). Purposeful sampling encompasses three broad strategies: (1) to achieve representativeness or comparability, (2) special or unique cases, and (3) sequential inclusion with the aim of generating theory (theoretical sampling). In mixed methods research, the sampling strategy should allow the researcher to draw inferences from both the qualitative and the quantitative data, thereby providing both depth and breadth (Teddlie & Yu, 2007).

3.1.3 Rationales for mixed methods

Common rationales for mixed methods studies are: (1) triangulation (seeking corroboration), (2) complementarity (seeking elaboration), (3) development (informing the other method), (4) initiation (discovering contradictions), and (5) expansion (seeking completeness) (Greene et al., 1989). A central concept is *triangulation*, adopted early on by Campbell and Fiske (1959). They proposed a “multitrait-multimethod matrix” whereby more than one quantitative method is used to measure a psychological trait. Denzin (1978) introduced the term triangulation for combining data sources to study the same social phenomenon. Triangulation has been broadly defined as the combination of two or more theories, data sources, methods or investigations in a single study of a phenomenon (Patton, 2002c). Morse (1991) outlined two types of triangulation: concurrent (simultaneous) and sequential. Three outcomes arise from triangulation: convergence, inconsistency, and contradiction. Thus, as different methods may yield confirming or contradictory findings, the fundamental issue is whether the findings are genuinely integrated, so that divergences may lead to new understandings.

Arguments for using mixed methods in psychiatric research have been the complexity of interventions and the need to identify their mechanisms of action, variations in the effect of interventions in sub-groups of people, and the necessity of incorporating patient perceptions of services (Crawford et al., 2002). An application is case-study research, which is recommended for the evaluation of health service interventions (Keen & Packwood, 1995; Yin, 2003).

3.2 ASSESSMENTS AND MEASURES

3.2.1 Measures

The DSM-IV and ICD-10 Personality questionnaire (DIP-Q). The DIP-Q is a self-report questionnaire for assessing the 10 DSM-IV and all 8 ICD-10 personality disorders (PDs) (Ottoosson et al., 1995). It contains 140 statements to be answered in a dichotomous form (true/false), 135 covering the criteria for specific PDs, and 5 covering the general criteria for a PD (the Impairment Distress Scale; the ID-scale). A comparison of the DIP-Q vs. a structured clinical interview found that agreement as measured by Cohen's kappa was 0.61 overall (Ottoosson et al., 1998). Only the DSM-IV entities were included in this thesis. For a detailed description, see Paper I.

The Inventory of Interpersonal Problems (IIP). The IIP is a self-report questionnaire measuring perceived interpersonal problems, originally constructed by Horowitz (1988). Weinryb et al (1996) made a Swedish translation of the 64-item version with eight subscales. The psychometric properties are presented in a manual with Swedish norms for patients and non-patients (Horowitz et al., 2002). The subscales have acceptable internal consistency and content validity. A general complaint factor is supposed to affect the individual scores. The eight subscales (domineering, intrusive, overly nurturant, exploitable, nonassertive, socially avoidant, cold, and vindictive) have associations to categorical and dimensional personality measures (Horowitz et al., 2002).

The Montgomery Asberg Depression Rating Scale – Self assessment (MADRS-S). The MADRS-S (Svanborg, 1999; Svanborg & Asberg, 1994; Svanborg & Åsberg, 2001) is the 9-item self-report version of the 10-item Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery & Asberg, 1979). The MADRS-S has high concordance with the expert-rated MADRS in samples with depressive and anxiety disorders. There are no systematic studies on clinical cut-off criteria for MADRS-S scores, but data from two normal samples and clinical observations indicate that a MADRS-S score of 12 or less signifies no depression.

The SCID-II Screen Questionnaire consists of 124 questions with a dichotomous answering format (yes/no), designed to cover the criteria for the DSM-III-R personality disorders (Ekselius et al., 1994). Ekselius et al. found that by raising the cut-off level for a PD by one criterion for every categorical diagnosis, the overall kappa for agreement between the SCID II interviews and the questionnaire with adjusted cut-off was 0.78.

The Structured Clinical Interview for DSM-IV Axis I Disorders, patient version with psychotic screen (SCID-I/P, version 2.0), is a semi-structured interview form for securing psychiatric diagnoses in research (First et al., 1997a).

The Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II) is a semi-structured interview form for diagnosing the 10 personality disorders in DSM-IV (First et al., 1997b). In this thesis, SCID-II interviews were guided by participants' reports on the screening instrument for Axis II. All participants were also interviewed for the criteria of depressive PD.

The Symptom Checklist-90/Brief Symptom Inventory. The self-reported Symptom Checklist (SCL) was originally developed 50 years ago as the Hopkins Symptom Checklist to serve as a 'discomfort scale' for neurotic distress (Olsen et al., 2004).

Derogatis modified the SCL to the 90-item versions SCL-90 and SCL-90-R (Derogatis, 1992; Derogatis & Cleary, 1977). The Brief Symptom Inventory (BSI) is a shorter version with 53 items, covering the same subscales and global indices as SCL-90 (Derogatis, 1992). There is strong evidence for using the mean total score of the SCL, the Global Severity Index (GSI), as an expression of overall neurotic illness (Olsen et al., 2004).

3.2.2 The Modified NIMH Life Chart Methodology

In his pioneering work, Kraepelin (1899/1921) instituted a systematic and detailed approach to patient care by longitudinally recording each patient's manic and depressive episodes, using a life chart. Life charts collect information about the long-term course of illness by using functional impairment as a measure of episode severity that can be corroborated by all available data from patients, diaries, their families, case records etc.

The Life Chart Methodology (LCM) was developed by a group at the National Institute of Mental Health (NIMH) for the delineation of the retrospective or prospective course of affective illness, as well as treatments and psychosocial stressors (Leverich & Post, 1992, 1998). The time domain for retrospective assessment is by month. Besides its use for bipolar disorder, the LCM has been employed in investigations of treatment-refractory affective disorders (Ehnavall & Agren, 2002), and temporal relationships between panic disorder and depression (Uhde et al., 1985). The Longitudinal Interval Follow-up Evaluation (LIFE) is the most widely used method for assessing the longitudinal course of psychiatric disorders with recommended assessments every six months (Keller et al., 1987). In this thesis, a modified retrospective NIMH-LCM was used because the long-term follow-up investigation was not initially planned in the original studies.

Some modifications of the LCM were necessary for the retrospective study of the illness course of dysthymia and panic disorder. Collection of retrospective data across the life-span presents many challenges, including potential for recall bias and concerns about the reliability and validity of the data collected. The modification draws on findings that autobiographical recall is enhanced by the use of self-generated thematic, temporal and visual information in Event history calendars (Belli, 1998; Lyketsos et al., 1994). Rich information from case records aided recall. As the course of dysthymia and panic disorder is characterised by fluctuating states, there was a need to develop an individual-specific scale that reflected the levels of illness. The method was adopted from Bilsbury and Richman (2002), who outlined a stage approach measuring patient-centred subjective outcomes.

Participants were asked to provide self-anchored descriptions of four illness-levels. Following a "Max-Min" procedure, they were instructed to start with the worst level, followed by the realistic minimum, and then the medium and low levels. Eliciting questions involved typical sensations in the body, feelings, thoughts, behaviours and function in work and in relations. I edited the words and phrases into the format of title and key descriptors, and assured that the levels corresponded to different levels of impairment: Level 4 "severe" (major depressive episode with functional impairments in several areas), Level 3 "moderate" (syndromal), Level 2 "symptomatic" (low functional impairment) and Level 1 with "no or minimal symptoms". The four levels were then used together with case-record data and a life event checklist according to the NIMH-LCM Manual. An example of self-anchored illness-levels is shown in Figure 1 in the Appendix.

3.3 PARTICIPANTS AND PROCEDURES

3.3.1 Paper I

Participants in Paper I were included between 1994-95 from three clinical populations (n=448) and healthy controls (n=139), see Table 3.

Participants from the general psychiatric population represented different clinical settings: psychiatric outpatients (22 %), general psychiatric inpatients (11 %), patients hospitalised after suicide attempt (38 %), and patients recruited from an inpatient assessment unit for sleep disorders (29 %).

Both forensic and psychotherapy-applicant populations were included consecutively, either for forensic examination or for assessment for psychotherapy. Psychotherapy applicants were recruited from the Stockholm Comparative Psychotherapy Study (S-COMPAS), from which also some participants in Papers II-IV were independently recruited. The healthy controls represented students in four classes at a college for medical care.

All participants self-reported personality with DIP-Q and the clinical populations were assessed by means of clinical diagnostic interviews with regard to Axes I, II and V (GAF) according to DSM-IV.

Table 3. Participant Samples in Paper I

Sample	n	Women, %	Age (years), Mean (SD)	Clinical Axis I diagnosis, %
Psychotherapy applicants (S-COMPAS)	94	81	34.2 (8.1)	Depression 56 % No Axis I 18 % Anxiety disorders 14 % Psychotic syndrome 3 % Various diagnoses 9 %
General psychiatric (Outpatients=22 %; Inpatients=78 %)	137	58	37.2 (12.0)	Depression 33 % Sleep disorder 18 % Anxiety disorder 15 % No Axis I 8 % Psychotic syndrome 7 % Various diagnoses 19 %
Forensic psychiatric	217	7	35.5 (10.3)	Alcohol/drug abuse/dependence 32 % Psychotic syndrome 26 % Depression 12 % Anxiety disorder 8 % No Axis I 8 % Various diagnoses 14 %
Healthy volunteers	139	69	28.0 (8.1)	-
Total	587			

S-COMPAS = the Stockholm Comparative Psychotherapy Study

3.3.2 Papers II-IV

Participants in Papers II-IV comprised psychiatric outpatients selected from two naturalistic treatment studies in Stockholm, the “S-COMPAS” and the “Solna Peptid-2” projects. They were included in the original studies 1992-96, and in the long-term follow-up investigation during 2004, see Table 4.

S-COMPAS (the psychotherapy study) aimed to develop methods for quality assurance of psychotherapy, and included 460 patients applying for publicly financed psychotherapy via psychiatric outpatient units in three separate areas of metropolitan Stockholm (Carlsson et al., 1996). Patients were included if they were regarded by the psychiatric assessment team as needing psychotherapy. Patients received different types of psychotherapy and many also received antidepressant medication. Evaluation of the treatment was performed after termination of psychotherapy, normally about 2 years after inclusion.

Solna Peptid-2 (the pharmacology study) included 48 patients at a general psychiatric outpatient unit with the aim of studying outcome and changes in the personality profiles and serum peptide levels of patients with dysthymia and panic disorder during two years treatment with SSRIs. Patients were included if they fulfilled the DSM-III-R criteria and accepted SSRI-treatment. They were informed that psychotherapy also might be considered at a later stage, if indicated. Some patients received concurrent psychotherapy. Data from this original study are not previously published.

The follow-up study. Participants were included in the follow-up investigation if: (a) dysthymia or panic disorder was the primary Axis I diagnosis, (b) illness duration was more than 2 years when included in the original studies, (c) not comorbid dysthymia and panic disorder, and (d) they had been evaluated with SCL-90/BSI before and after the original studies. Totally 83 patients fulfilled these criteria, of whom 42 (51 %) accepted to participate in the follow-up investigation. The selection process and flow-chart are described in more detail in Paper II.

Table 4. Participant Samples in Papers II-IV

Sample	Diagnosis	Paper II		Paper III		Paper IV			
		2-year PT	9-year FU	2-year PT	9-year FU	2-year PT	9-year FU		
		N	Women, N (%)	N	Women, N (%)	N	Women, N (%)		
S-COMPAS	Dysthymia	29	20 (69)	16/15	11 (69)	15	10 (67)	7	5 (71)
	Panic disorder	19	15 (79)	7/5	4 (57)	5	3 (60)		
Solna Peptid-2	Dysthymia	15	6 (40)	9/8	3 (33)	8	3 (38)	3	1 (33)
	Panic disorder	20	14 (70)	10/10	6 (60)	10	6 (60)		
Total		83	55 (66)	42/38	23 (55)	38	22 (58)	10	6 (60)

PT = Post-treatment

FU = Follow-up

Incl. = Included in analysis due to fulfilled criteria for dysthymia or panic disorder

S-COMPAS = the Stockholm Comparative Psychotherapy Study

Solna Peptid-2 = the pharmacology study

All participants had self-assessed their personality with the SCID-II Screen Questionnaire or the DIP-Q, and their psychiatric symptoms with SCL-90 or BSI before and after the original studies. In the Solna Peptid-2 study, an experienced psychiatrist (PS) performed the SCID-I and the SCID-II interviews. The diagnoses in the S-COMPAS study were controlled by an experienced psychiatrist (CS) with use of all available data, including correspondence between cut-off scores for screening instruments for Axis II, clinical diagnoses and check-lists with DSM-IV criteria for Axis I disorders.

In the follow-up investigation, participants self-reported personality with DIP-Q, symptoms with BSI and consented to collection of all available case records. CS performed individual interviews with all participants, starting with SCID-I & -II interviews, guided by DIP-Q. This was followed by life-charting interviews and in-depth interviews. Interview guides are described in Papers III-IV. Four of 42 participants had a primary lifetime Axis I diagnosis other than dysthymia or panic disorder and were therefore excluded from further analysis. Diagnostic evaluations at follow-up were discussed with the primary investigator of the Solna Peptid-2 study (PS).

Definitions for outcome were set a priori, using a time interval of six months prior to follow-up. *Remission* and *Partial remission*: Patients did not meet DSM-IV criteria for dysthymia or panic disorder, the former having only minimum symptoms, the latter having some symptoms or functional impairments. *Non-remission*: Patients were meeting DSM-IV criteria for dysthymia or panic disorder.

Paper IV comprises a subsample of the 38 participants in Papers II and III. Ten patients with persistent dysthymia were purposefully selected for a multiple-case study design. Each case was defined as all information about a single patient's health-related behaviour and interactions. The prime unit of analysis consisted of statements concerning patients' and providers' understandings of illness and negotiations of care in case records. The study used all available data concerning these individuals.

3.4 ANALYSIS

3.4.1 Statistics

The statistical analyses in Papers I-IV were performed using the SPSS program. The following statistical tests were used.

In Paper I: Student's t-test, chi-square test, logistic regression.

In Paper II: Student's t-test, chi-square test, Mann-Whitney's U-test, ANOVA, ANCOVA.

3.4.2 Qualitative content analysis

Qualitative content analysis was used in Papers III-IV. Qualitative research methods involve the systematic collection, organisation, and interpretation of data derived from interviews, observations and documents (Malterud, 1998). In the follow-up investigation we wanted to understand the various experiences of the participants and chose to use qualitative content analysis (QCA) because all data were collected concurrently and analysed afterwards. QCA should be distinguished from the quantitative content analysis that deals with the counting of manifest content in categories predetermined by the researcher (Silverman, 2001). Manifest content describes the visible components, whereas latent content involves a co-construction of the participant's reality and subjective interpretation by the researcher (Graneheim & Lundman, 2004).

The analytic procedure shares basic elements with grounded theory and phenomenology in that it involves the identification of meaning units, initially staying close to data by open coding, as well as condensation and abstraction of the content by constant comparisons (Malterud, 1998; Strauss & Corbin, 1998). A primary team (co-coders and I, see Papers III-IV) performed coding in order to handle preconceptions and to stay open to multiple interpretations of the data. Comparisons were aided by the use of the software NVivo 2.0. We checked for rivaling interpretations and re-contextualised the categories and subcategories by re-reading and comparing coded interviews with all available data in case records, life-charts and observations in field notes. The analysis comprised elements of Consensual Qualitative Research (Hill et al., 2005), using frequency labels in the cross-analysis and an external auditor.

The data reduction and sense-making process can be described as a condensation of meaning units into manifest and latent content and further into subcategories and categories (Graneheim & Lundman, 2004). Two examples of the process are shown in Tables 5 and 6 in the Appendix. The second example concerns an extreme case with low communication ability and contains contradictions of content in the interview with case records, field notes and life-charting. The analysis of this case accordingly involved a higher degree of abstraction in the interpretation. This matter will be further discussed.

3.4.3 Case study research and theoretical framework

In Paper IV, a theory-testing and explorative multiple-case study design was used with developmental cognitive theory as framework. During the preparation of the follow-up investigation I was interested in how patients understand their illness and included a question on this matter in the interview guide. However, I had not originally planned to analyse case records. Finding difficulties in negotiating treatment attracted my interest to the interaction between patients and providers.

An insight from the interviews had been that patients' understandings of illness varied hugely with regard to content and language structures, and that the content might be conflicting. Besides explanatory models involving cause-effect relationships, we had noticed that illness perceptions often were communicated with analogical reasoning in metaphors or concrete imagery. The literature on patients' illness perceptions was scrutinised to find a theoretical model, e.g. (Bhui & Bhugra, 2002; Kleinman, 1978). Based on the ideas of the anthropologist Allan Young, Stern & Kirmayer (2004) had described a scheme for analysing knowledge structures in illness narratives that we found appropriate for our purpose. Allan Young had proposed that many persons use a concrete, perceptually bound understanding of illness which affects the negotiations in the clinical encounter (Young, 1981). He draws on the writings of J. Piaget about preoperational thought processes, and on C. R. Hallpike about transductive reasoning, i.e. moving from particular (prototype) to particular (experiential referent). Preoperational thinking is characterised by concrete, perceptually bound understanding and centration (focusing on or attending to only one aspect of a stimulus or situation). Other forms of analogical reasoning involve associations of elements (symptoms, emotions, behaviours, etc) into 'chain-complexes' on the basis of their contiguity. The model has resemblances to associative learning theories (Bouton et al., 2001). We added the categories sensori-motor accounts and metaphors to the coding scheme of Stern & Kirmayer, and used cognitive developmental theory as a theoretical framework that was tested and explored in a multiple-case study design.

Yin (2003) has defined case-study research as a design that: (1) investigates a phenomenon within its real-life context, especially when the boundaries between phenomenon and context are not clearly evident; (2) relies on multiple sources of evidence, with data needing to converge in a triangulating fashion; and (3) benefits

from prior development of theoretical propositions to guide data collection and analysis. Multiple cases should be selected so that they may replicate each other by obtaining similar results or contrasting results for predictable reasons, thus providing a ground for analytic generalisation. We used all available data to test the proposition that patients' understanding of illness in concrete, perceptually bound (preoperational) knowledge structures contributed to 'Failed negotiations', defined as incongruence between patients and providers leading to dropout before remission. The analysis comprised qualitative content analysis and a coding scheme of knowledge structures. The coding scheme is presented in Paper IV.

4 RESULTS

4.1 PAPER I. VALIDITY OF THE DSM-IV AND ICD-10 PERSONALITY QUESTIONNAIRE (DIP-Q)

The aim of the study was to examine the validity of personality diagnosing by means of the DSM-IV and ICD-10 Personality Questionnaire (DIP-Q) in three clinical samples and healthy controls in relation to clinical and demographic factors. The prevalence of PDs according to DIP-Q was 14 % in healthy volunteers, compared to 59 % in the general psychiatric sample, 68 % in the forensic sample and 90 % among psychotherapy applicants. Multiple DIP-Q PDs were common in all clinical samples, the mean number ranging from 2.33 (general psychiatric sample), 2.95 (forensic sample), to 3.31 (psychotherapy applicants). PDs were more prevalent among women.

The rates of DIP-Q PD were further examined with multivariate analyses due to differences in the distribution of clinical Axis I diagnoses and gender among the clinical samples. The strongest factors associated with a DIP-Q diagnosis were clinical group and depressive disorder. However, when adjusting for depressive disorders, the forensic psychiatric and the psychotherapy applicants were still twice and five times as likely to receive a DIP-Q PD diagnosis as the subjects in the general psychiatric sample. The influences of female gender and comorbid anxiety disorder were not significant in the multivariate analysis. However, tendencies toward an increased probability of DIP-Q PD in connection with anxiety disorder and female gender remained.

DIP-Q dimensional scores differed between the clinical samples. Compared to the general psychiatric sample, the psychotherapy applicants fulfilled more criteria in clusters B and C, and the forensic psychiatric patients in clusters A and B. Concerning specific PDs, the psychotherapy applicants scored higher on the borderline and all cluster C PDs, and the forensic patients scored higher on antisocial PD. All clinical groups differed significantly from the healthy volunteers in all cluster dimensions.

The high association between DIP-Q personality disorder and depression could result from true comorbidity, but could also be a state-dependent effect. The high prevalence among psychotherapy applicants is probably most related to severe psychopathology, but may also be influenced by awareness of problems and help-seeking behaviour. In diagnosing personality disorder with the DIP-Q, caution is recommended for these factors.

4.2 LONG-TERM OUTCOME OF PATIENTS WITH DYSTHYMIA AND PANIC DISORDER: A NATURALISTIC 9-YEAR FOLLOW-UP

4.2.1 Paper II. Stability of change and impact of comorbid PD

The aim of this study was to examine the long-term outcome of standard treatments for patients with dysthymia and panic disorder, without confusing early-onset dysthymia and secondary depressions. In 2004, 83 patients with dysthymia and panic disorder were asked to participate in a long-term follow-up of naturalistic studies with antidepressants and psychotherapy. Forty-two (51 %) agreed to participate, of whom 38 fulfilled inclusion criteria at follow-up (dysthymia, n=23; panic disorder, n=15). There were no differences between participants and non-participants regarding age, sex, Axis I diagnosis, frequency of comorbid Axis II diagnosis, symptom level at baseline and

after 2 years. Participants were therefore assessed as being representative of all 83 patients.

At the 9-year follow-up, 26 % (n=6) of patients with dysthymia and 20 % (n=3) of patients with panic disorder were in remission as defined by SCID-I-interviews, the time criterion of six months, and symptom measures. According to the life-charting, they had been in remission for 1-8 years (median 4 years). Including partial remission individuals, 57 % (n=13) of patients with dysthymia and 47 % (n=7) of patients with panic disorder were improved.

At baseline of the original studies, both diagnostic groups had a high degree of comorbidity with anxiety disorders and PDs, predominantly in Cluster C (avoidant, obsessive-compulsive, dependent), and high rates of reported childhood adversities (about 80 %). Patients with dysthymia differed in that they had a higher frequency of PDs (74 % vs. 40 %), earlier age of onset (14 vs. 24 years old), longer illness duration (23 vs. 7 years) and were older (37 vs. 31 years old).

The stability of change compared to the 2-year outcome and the influence of comorbid PD at baseline was tested with a three-way ANOVA with the symptom measure GSI as within repeated dependent factor and the diagnostic groups and PD as between factors. The analysis showed that comorbid PD was a negative prognostic factor irrespective of Axis I diagnosis and post hoc tests showed that patients with panic disorder had deteriorated compared to the 2-year outcome. Testing for possible confounding of age and GSI level at baseline with an ANCOVA confirmed the results.

The low remission rates elucidate the consequences of undertreatment. The less stable outcome for patients with panic disorder suggests that standard treatments are not resulting in enduring remission.

4.2.2 Paper III. Perceived helpful and hindering factors to remission

The aim of this study was to examine the phenomenon of remission by investigating the perceptions of patients with dysthymia and panic disorder with different long-term outcomes at 9-year follow-up. Specifically, we wanted to explore: (1) perceived helpful and hindering factors, (2) common and specific factors, and (3) convergence between patients' subjective views on remission with objective diagnostic assessments.

The comparative cross-analysis concerning perceived helpful and hindering factors to remission resulted in both common and specific categories for participants with dysthymia and panic disorder. The subjective perceptions about life today, change and the future were generally convergent with diagnostic outcome criteria. General for participants in remission were perceptions of having received 'Tools to handle life', which had built a sense of empowerment and optimism about the future. As an illustration, a quotation from a man with former dysthymia is included:

How do you cope with strains in life today? "...I think that I have become better at making distinctions... (laughs)..., yes, it's difficult to describe it in another way, to be able to differentiate cause and effect and things that just trigger old patterns for survival. I mean a strategy that I created over the years. I don't want to use it now. I can recognise it in situations that earlier on automatically triggered a certain behaviour or way of thinking. Now I feel that I can stop myself and see that it belongs to the past. () And what I mean with the old strategies is to withdraw, or not participate in things to avoid having troubles."

Common helpful factors were enhanced understanding of self and illness mechanisms, antidepressant medication, confidence in the therapist, enhanced flexibility of thinking, and social support from friends and family. The most common

and almost general hindering factor was difficulty in negotiating treatments (defined as access problems), especially to receive psychotherapy. Successful negotiations, defined as overcoming access problems by fighting for requests, were typical for participants in full or partial remission. In contrast, non-remitted participants with PDs had problems expressing their needs. Other common hindering factors were medication problems, lack of confidence in the therapist, lack of understanding of illness, and unresolved relational problems. The only category that could be linked to a specific psychotherapy was perceptions of the therapist as too non-directive, associated to psychodynamic psychotherapy.

Participants with panic disorder and dysthymia described specific helpful relationships to the therapist, irrespective of type of psychotherapy or outcome. In panic disorder this was described as good collaboration, 'Therapist as coach'. A general helpful factor for those in remission was enhanced capacity to identify, tolerate and handle feelings, whereas non-remission individuals had difficulty handling bodily sensations and feelings. Other helpful factors were relaxation techniques and exposure. Fear of anxiety and phobias were other hindering factors.

In dysthymia, the helpful relationship to the therapist was described as a caring relation, 'Therapist as parent'. General helpful factors for those in remission were learning self-acceptance and compassion, resolved relational problems, and having been helped by several psychotherapies. Other helpful factors were experiential and creative techniques, and feedback from others in group therapies. Hindering factors were mistrust of others, blaming self or others when there were problems, difficulties in close relations, and sensitivity to confirmation.

I propose a general model for enduring remission from dysthymia and panic disorder, including understanding self and illness mechanisms, enhanced flexibility of thinking, and change from avoidance coping to approach coping; and that a helpful relationship to the health care provider is a vehicle for this change. In addition, each diagnostic group seems to need specific treatment ingredients. A mechanism for recurrence of panic disorder might be that treatments which help patients with panic disorder to avoid or control sensations are ineffective in the long run. Low capacity to negotiate treatments may be one reason why comorbid PD is a negative prognostic factor in naturalistic studies.

4.3 PAPER IV. BARRIERS IN THE HELP-SEEKING PROCESS

The purpose of this study was to investigate barriers to diagnosis and adequate treatment of patients with early-onset dysthymia. We proposed that patients' understanding of illness in preoperational knowledge structures (concrete, perceptually bound structures) contributed to 'Failed negotiations', defined as incongruence between patients and providers leading to dropout before remission. Rival explanations could be providers' attitudes, factors associated to comorbid PD, or contextual factors (e.g. organisational issues). Data pertaining to 10 non-remission dysthymic patients were analysed from: (1) case records (statements concerning patients' and providers' understandings of illness and negotiations in case records as prime units of analysis), (2) self-assessments (MADRS-S, DIP-Q, IIP), and SCID-II interviews, (3) interviews, (4) observations recorded in field-notes, and (5) life-charting of illness course, treatments and life events.

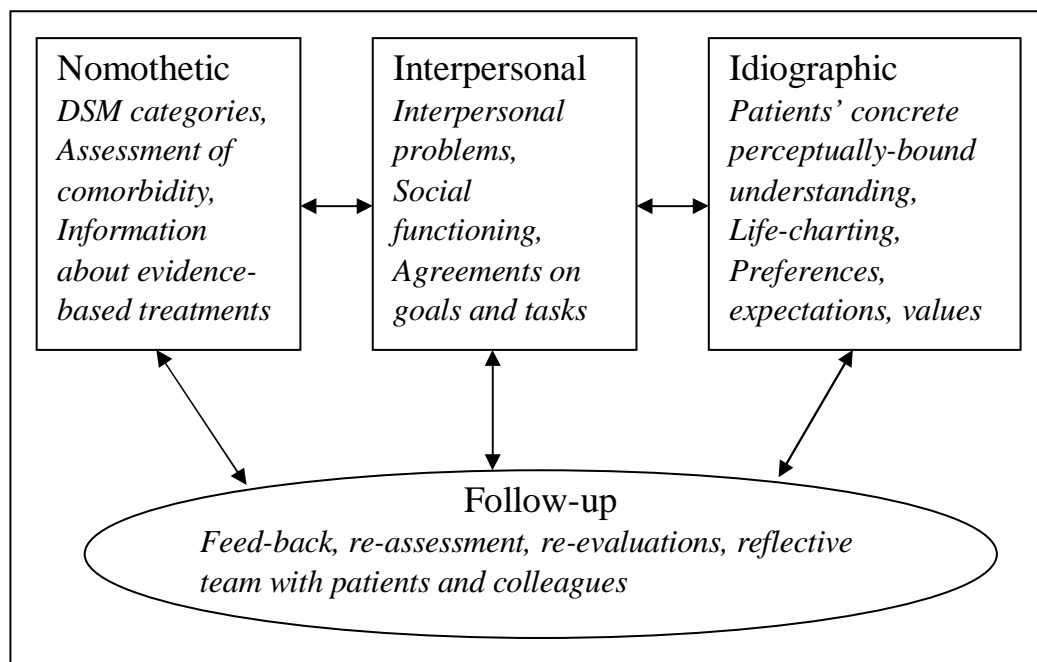
The main proposition was supported by two patterns. Patients expressed dysthymia with sensori-motor accounts (bodily perceptions or actions) in childhood and adolescence; providers focused on somatic problems. After adolescence, patients expressed dysthymia with a complexity of aspects, including concrete, perceptually

bound understanding like metaphors and prototypical experiences; providers focused on one aspect, usually relational problems, and overlooked other aspects. A modification of the model is that providers' cognitive errors contribute to failed negotiations.

However, there was also evidence for the rival propositions that providers' attitudes, contextual factors and comorbid personality disorder contributed to failed negotiations. Patients' requests had been rejected or treatments terminated due to providers' attitudes, e.g. about limit-setting and negative beliefs about combinations with antidepressant medication and psychotherapy. Contextual factors were missed modifications of treatment plan due to lack of follow-up, and problems with access to psychotherapy.

A key barrier was the pattern of patients' strategy of concealing due to fear of rejection and mistrust, thereby contributing to misdiagnosis, dropouts and hindering change. Another pattern was patients' problems with handling conflicts, mainly by non-assertiveness. The patterns were convergent with assessments of PD and interpersonal problems, which suggests that these two patterns are associated to comorbid PD. I suggest that Cluster C traits and dysthymia are conceptually intertwined, i.e. that fear of rejection and mistrust with the associated strategy of concealing is a key mechanism in driving persistence of the disorder.

A theoretical model that involves patients' understanding of illness in preoperational thinking and providers' cognitive errors can explain communication barriers. To overcome the barriers and attain shared decision making (SDM), I suggest that shared understanding is necessary in four areas, as shown in Figure 2.



The arrows indicate that understanding is developed by interaction of different knowledge areas, the centrality of interpersonal functioning and the need of continuous follow-up

Figure 2. Suggested Necessary Areas of Shared Understanding and Treatment Planning with Dysthymic Patients

5 DISCUSSION

5.1 FACTORS INFLUENCING THE VALIDITY OF THE DIP-Q

Paper I showed that personality disorder evaluated by means of the DIP-Q discriminated between different clinical populations and healthy controls. Interview-based studies of the general population in the United States ($n=43\ 093$) and Norway ($n=2\ 053$) have found a prevalence of any PD of 15 % and 13 %, respectively (Grant et al., 2004b; Torgersen et al., 2001). In Sweden, an investigation with the DIP-Q in a community sample ($n=557$) found a prevalence of 11 % (Ekselius et al., 2001). The 14 % rate of self-reported PD among healthy volunteers in the present investigation corresponds well with these findings. The slightly higher prevalence in this study compared to the other study with DIP-Q may be due to the younger age of the apparently healthy college students recruited (mean age: 28 vs. 42), as rates of PDs decline in the late 20s (Cohen et al., 2005).

General problems with self-assessments of PDs are the sensitivity to state-effects and that they are overinclusive in diagnosing personality disorders (Zimmerman, 1994). The DIP-Q includes an impairment and distress scale (the ID-scale) and a self-reported version of the Global Assessment of Functioning (GAF) scale, assessing the general criteria for PD. The ID-scale and self-reported GAF <70 set the threshold for a categorical diagnosis. Thus, it seems that summing these measures makes the instrument less overinclusive and gives good estimates for the presence of a PD.

The primary aim was to examine the validity of the DIP-Q in relation to setting and the influence of demographic and clinical factors. The dimensional cluster scores and to some degree also patterns of specific categorical Axis II diagnoses distinguished between the clinical samples. Compared to the general psychiatric sample, the psychotherapy applicants fulfilled more criteria in total and in Clusters B and C, and the forensic sample had higher scores in Clusters A and B. With regard to specific PDs, the psychotherapy applicants had higher frequencies of PDs in Cluster C and of Borderline PD, and the forensic sample had a higher frequency of antisocial PD. The DIP-Q has later been translated and validated in a Danish sample, as well as compared to Swedish samples of substance abusers (Hesse, 2005). Further, that study found that a 4-factor structure of the DIP-Q is invariant over the Danish and Swedish samples. The four factors introversion, antagonism, neuroticism and conscientiousness loaded on Clusters A, B, avoidant/dependent PDs and obsessive-compulsive PD, respectively. Altogether, it seems that the dimensional structure of PDs comes closer to the true nature of personality pathology.

The prevalence of any PD in the general psychiatric and forensic samples was as expected (Alnaes & Torgersen, 1988; Holmberg, 1994; Zimmerman et al., 2005). However, the most intriguing finding was the high prevalence of PDs among applicants for psychotherapy (90 %). The multivariate logistic regression helped to adjust for the influence of Axis I diagnoses, age and gender. The high prevalence is probably most closely related to severe psychopathology, as another study of participants in the S-COMPAS project showed a higher degree of psychopathology, indicated by the Rorschach test, compared to general psychiatric outpatients (Carlsson et al., 1996). The Rorschach test is not a self-assessment method for evaluating personality and thus not influenced by the same types of response sets. Awareness of problems and help-seeking behaviour may also have an influence. Applicants for psychotherapy seek help for often persistent problems and have at least an emerging

awareness of problems that motivates help-seeking. Typically, they exhibit internalising symptoms with a tendency to self-blame. Moreover, they may have been motivated by the opportunity to receive publicly-funded psychotherapy. These factors need to be acknowledged because the interpretation of test results should be informed by all types of 'test-taking behaviours' (American Educational Research Association, 1999).

The high association between DIP-Q personality disorder and depression could result from comorbidity, but might also be a state-dependent effect. The strong association between depression and personality, e.g. common dimensional traits of high neuroticism and co-occurrence, has led researchers to question the possibility of disentangling these concepts (M. H. Klein et al., 1993). In prospective investigations across childhood and adulthood, it appears that Axis I and Axis II disorders reinforce each other when they co-occur (Cohen et al., 2005). The DIP-Q measures a negative self-concept that can be a state-effect of a depressive episode or long-lasting traits of perceived inadequacy. The sex differences in the present study are in accordance with other reports. Women have elevated rates of affective and Cluster C disorders, and men have elevated rates of substance use and antisocial personality disorders (Grant et al., 2004a; Wittchen & Jacobi, 2005). In congruence with most self-report questionnaires, women had higher severity ratings.

A limitation of the study was that the results have not been compared to interview-based assessments of PD, which might have clarified some state-effects. To conclude, the DIP-Q seems to be a valid and useful instrument for diagnosing personality disorders in clinical practice. Moreover, it has been reported that the DIP-Q has predictive validity for recidivism in forensic samples (Hiscoke et al., 2003) and traumatic stress among soldiers (Michel et al., 2005). However, caution is recommended for the effects of depression, patients' degree of awareness and the clinical context.

5.2 RECOVERY FROM DYSTHYMIA AND PANIC DISORDER

5.2.1 The follow-up

Papers II and III present findings from a 9-year follow-up investigation of 23 patients with dysthymia and 15 patients with panic disorder. We selected patients with long illness duration and non-comorbid dysthymia and panic disorder, based on the assumption that a lack of differentiation between primary, early-onset dysthymia and secondary depressions may be a confounding factor in the study of outcome and influence of comorbid PD. Furthermore, we wanted to compare the perceptions of the diagnostic groups regarding helpful and hindering factors to enduring remission, and contrast them to objective measures.

The study comprises a small, non-random sample for quantitative analyses, and a large sample for qualitative analyses. Doubling the sample sizes would have conferred greater confidence in the outcome findings but the present sizes are sufficient for the qualitative analyses. This illustrates some of the challenges facing concurrent mixed-methods research, which are not present in sequential designs. The retrieval rate was also relatively low, although satisfactory in relation to the follow-up after 9 years. Thus, a major question is whether the findings can be generalised and are applicable to other patients with dysthymia and panic disorder. The participants were, however, judged to be representative of all the 84 patients recruited from psychiatric care and had typical clinical and demographic characteristics. Patients with panic disorder had lower rates of comorbid PD than expected, which may be a result of excluding cases with comorbid dysthymia. Methodological strength is the prospective,

longitudinal design with careful assessments, detailed life-charting and combined methods, which is indicative of the findings validity.

The recovery rates are in accordance with other naturalistic long-term follow-up investigations of early-onset dysthymia and panic disorder with agoraphobia. About 50 % showed substantial improvement, of whom 25 % had been in full remission for a median of 4 years. Also consistent with other studies, we showed that comorbid personality disorder predicted a persistent course irrespective of Axis I diagnosis. Patients had long illness duration and a high frequency of childhood adversities, which are known factors for persistent course. We investigated the impact of the categorical diagnosis of a PD, i.e., that a patient was assessed to fulfil the general criteria of having inflexible, enduring traits defining maladaptivity. An alternative would have been to use maladaptive traits dimensionally, which may be a more valid measure of severity than a categorical diagnosis. However, assessment of the general criteria for any PD (see p. 3) seems to have clinical relevance; and as the patients had not originally self-assessed personality with the same instrument, this could not be used for prediction. Furthermore, we found that patients with panic disorder had a less stable outcome, despite having received evidence-based treatments with good effect in the original studies, lower frequency of comorbid PD and shorter illness duration. Detailed life-charting and rich access to case records revealed that patients with dysthymia often had received subtherapeutic doses of antidepressant medication and that non-remitted panic patients had received less psychotherapy. Our observational design and small sample size made it hard to draw conclusions from these observations. However, it is reasonable to assume that undertreatment contributed to persistence and recurrence (Howard et al., 1996; Masand, 2003). The qualitative analysis in Paper III sought to reach a deeper understanding of the findings of the less stable outcome of patients with panic disorder and the negative impact of comorbid PD.

5.2.2 Options for recovery

The qualitative analysis suggests a general model for recovery from dysthymic and panic disorders involving: (1) understanding self and illness mechanisms, (2) enhanced flexibility of thinking, (3) change from avoidance coping to approach coping, and that a helpful relationship to the health-care provider is a vehicle for this change. The model is supported by other findings, e.g. the links between avoidance coping and stress generation (Holahan et al., 2005), and the effects of cognitive and emotional suppression in experimental studies (Wenzlaff & Wegner, 2000). Furthermore, it has been suggested that avoidance of reactivating distressing autobiographical memories is a vulnerability factor for relapse in depression (Brewin et al., 1999).

An enhanced understanding and a helpful relationship are ingredients that are consistent with the 'common factors' in treatment and research on clients' experiences of psychotherapy (Elliott & James, 1989). For example, an earlier explorative study on patients' perceptions of helpful factors found that understanding and advice were most related to short-term outcome (Murphy et al., 1984). However, different approaches of psychotherapy and biological psychiatry have varying explanatory models with a variable fit among patients, i.e., they may have specific content. For example, some patients prefer understanding of illness on the level of neurobiological changes in stress systems, whereas others prefer understanding of behaviours. Recovered patients described that they had achieved an understanding that facilitated behaviour change from avoidance to approach coping.

Patients with dysthymia and panic disorder have high frequencies of avoidant and obsessive-compulsive disorders (and traits), as well as core symptoms of social withdrawal and agoraphobic avoidance. The behavioural patterns of avoidance and control can be viewed as maintaining mechanisms that need to be targeted in order

to attain enduring remission. This implies that these behaviours need to be included in routine assessments in the same way as depressive and anxious symptoms. This is essential, as maintaining behaviours are connected to the pathological process and contribute to functional impairments. When patients achieve self-understanding and learn more adaptive behaviours, they perceive self-efficacy (Bandura, 2004). This was consistently expressed by recovered participants as “now I have the tools to handle life”.

Specific factors were perceived as being important for the diagnostic groups but only one factor could be linked to a specific type of psychotherapy (the therapist too non-directive in psychodynamic psychotherapy). Research aimed at comparing patients’ perceptions of different types of psychotherapy has found some differences, e.g. that patients may view the therapist as too passive in psychodynamic psychotherapy and too actively demanding in cognitive-behavioural therapies (CBT) (Nilsson et al., 2007). Common aspects of treatment were reported most frequently in a comparison of perceived helpful factors between CBT and interpersonal therapy, however, CBT techniques were specific for the group receiving this treatment (Gershefski et al., 1996). The present study had neither the purpose of comparing therapy approaches nor that design, but aimed to capture perceptions of helpful and hindering factors to enduring remission, irrespective of ‘brand-names’. The different key areas for change, handling of feelings vs. self-acceptance/resolution of relational problems, are in line with the tripartite model (Clark & Watson, 1991) and evolving treatment models. More surprising was the finding of dissimilar descriptions of the therapists, which generated the hypothesis that dysthymic patients are in greater need of interventions that target their unmet needs for attachment, interpreted as the alliance factor ‘bond’. Traditionally this is considered to be a ‘common’ factor for all types of treatment and patient (Horvath & Bedi, 2002). The finding from the present explorative study that the factor ‘bond’ may have a specific curative effect for patients with early-onset dysthymia needs further investigation.

The treatment ingredient enhanced flexibility of thinking can be connected to different concepts and types of psychotherapy, e.g. ‘metacognition’ and ‘decentration’ for cognitive-behavioural relapse prevention of depression (Fresco et al., 2007; Teasdale et al., 2002), development of ‘reflective functioning’ in psychoanalytically informed treatment of borderline personality disorder (Fonagy & Target, 1996), and ‘formal-operational thinking’ in normal cognitive maturation (Elkind, 1981). Enhanced flexibility of thinking is an awareness of the cognitive content that may be summarised as “Thoughts are not facts” (Segal et al., 2002), an ability that may reduce the need for avoidant cognitive processing. Social support and meaningful relations (including becoming a parent) seem to be a common factor that promotes recovery from various mental problems, provided the relationships are manageable. An implication for health care is to pay attention to the social network in treatment. Patients’ perception that antidepressant medication is both helpful and problematic was expected. For example, it has been suggested that antidepressants have an effect on the common factor of negative emotionality (neuroticism) according to the tripartite model (Shelton & Brown, 2001). With reference to the differential effect of combination treatments in panic disorder and dysthymia, antidepressant medication may have a specific effect on depressive illness.

The model of factors for recovery can be questioned for seeking supporting evidence that leads to confirmation bias, instead of seeking evidence that may falsify the model. Another limitation is that the model is based on a limited number of participants, possible memory bias and the intersubjective nature of the inquiry. At the current state of knowledge, however, I suggest that it is necessary to

identify key elements for recovery and formulate models that can be tested in different contexts. Other methodological concerns are discussed in Paper III.

5.2.3 Obstacles to recovery

The perceived main obstacle was difficulty in negotiating treatments; many non-remitted participants described explicitly that they had not been able to overcome access barriers. Negotiation is a key concept in the comprehension of the functions of language. Negotiation denotes a specific type of dialogue that aims at bargaining agreements which may satisfy both parties to an action. Negotiation is also a concept for describing and explaining dialogic interaction, e.g. used by Safran and Muran (2000) in understanding therapeutic alliance as an ongoing negotiation process. Non-remitted patients with PDs had more difficulties in expressing needs. The finding in the present study suggests that low capacity to negotiate and adhere to treatments might contribute to the negative impact of comorbid PD in long-term follow-up investigations. Some participants had communication problems also in the interview that illustrated a low capacity to express requests.

One example is the excerpt from the qualitative content analysis of a man with persistent dysthymia (see Appendix, Table 6). The contrasting example in the Appendix (Table 5), illustrates how capacity to negotiate treatment is dependent on awareness and determination. The transcript of the man with persistent dysthymia was very meagre, contradictory and difficult to understand without additional information. Without triangulation, using rich access to case records and other information, it would have been hard to analyse the transcript. Latent content had to be interpreted in order to co-construct implicit meaning. The analytical process adheres to the standards for qualitative research (Elliott et al., 1999; Morrow, 2005). My standpoint is that the procedure gives a deepened understanding of obstacles in ordinary care that would be missed by only coding manifest content or the use of questionnaires.

Communication problems may also be one reason for subtherapeutic doses of antidepressant medication. Evidence suggests that patients with PDs are less likely to receive drugs in ordinary care and that the effect of PD on depression outcome is least in well-structured treatment programs (Mulder, 2002). In the present study, participants perceived difficulty in receiving psychotherapy. Reports suggest that the addition of psychotherapy reduces dropouts in longer therapies (Pampallona et al., 2004). Thus, there are many reasons for actively paying attention to patients' treatment preferences. The finding of communication problems is based on a small number of participants. However, I suggest that the finding is applicable to other settings but may vary in degree with the type of PD and setting. A clinical implication is that to attain enduring remission, comorbid PD needs to be assessed and addressed.

The perceived specific hindering factors for the diagnostic groups corresponded well with the reported helpful factors. Non-remitted patients with panic disorder described controlled re-breathing and other measures to control sensations. The finding is consistent with research suggesting that treatments that incorporate affect control strategies, e.g. relaxation, distraction and benzodiazepine use, are less efficacious over time than exposure-based procedures (Fava et al., 2001; Otto & Deveney, 2005; Schmidt et al., 2000). The analysis suggested that a mechanism for recurrence of panic disorder might be that treatments that help patients to avoid or control sensations are ineffective in the long run. This is of special interest, as health care providers need to be aware of that ingredients of treatment may be obstacles to long-term remission.

5.3 OBSTACLES TO RECOGNITION AND TREATMENT

In Paper IV we studied how understandings of illness by dysthymic patients and their providers had evolved and how treatments had been negotiated over time. As described in the methods section, the choice of a multiple-case study design and the theoretical framework of developmental cognitive theory emerged from the observations in the follow-up investigation.

Case-study design is recommended for the evaluation of complex health service interventions when there is no control of events, e.g. to examine how and why interventions succeed or fail (Keen & Packwood, 1995). It may address questions with relevance for everyday clinical practice, thus bridging the research-practitioner gap. However, the method is challenging as the data are complex and “there is no single correct method for doing case studies” (Stiles, 2007, p. 122). Experts on case-study research, e.g. Yin (2003), stress the role of theory, rival explanations and rich case descriptions that facilitate judgements of correspondence between theory and observations. The notion of analytical generalisation implies that if two or more cases support an appropriately developed theory, replication may be claimed. The choice of theoretical framework was based on prior knowledge in cognitive theory, observations of analogical reasoning, and the writings of Allan Young about preoperational knowledge and transductive reasoning (1981), which altogether could be applied in a modified coding scheme. In line with case-study design, the prime units of analysis were explicitly defined as statements concerning patients’ and providers’ understandings of illness and negotiations of care in case records; other sources were used to corroborate and contradict the findings.

Failed negotiations could be explained by communication problems. Patients had mainly expressed illness with concrete bodily sensations, metaphors, prototypes or chains of events, which confirmed the theory that patients with early-onset dysthymia express illness in preoperational knowledge structures according to the terminology of Piaget. The failures were characterised by providers focusing on a single aspect instead of on the complexity of presented illness cognitions. Thus, cognitive theory was useful for the understanding of communication barriers between patients and providers.

However, we also found support for the rival propositions that providers’ attitudes, comorbid personality disorder and contextual factors like lack of follow-up contributed to failed negotiations. The pattern associated to comorbid PD of concealing due to fear of rejection, mistrust and problems with conflicts suggests that Cluster C traits and early-onset dysthymia are conceptually intertwined. This is suggested to be a key mechanism in driving the persistence of the disorder by contributing to vicious circles in interpersonal communication. This hypothesis is supported by research on cognitive aspects of chronic depression and that Cluster C personality disorders are most predictive for chronic depression, with increasing withdrawal over time (Iacoviello et al., 2007; Paris, 2003; Riso et al., 2003).

Further, we found that patients’ understanding in concrete, perceptually bound language structures and narratives elicited by the life-charting interview provided essential information not captured by diagnostic interviewing. Metaphors and imagery seem to communicate specific types of comprehension, e.g. shown by fMRI studies (the reading of metaphors leading to higher activation in several brain areas than irony and literal statements) (Eviatar & Just, 2006), and overviews on mental imagery and memory in psychopathology (Hackmann & Holmes, 2004). We interpreted that providers had failed to use and develop these knowledge structures due to cognitive errors, i.e. the use of selective attention. However, there are always alternative interpretations of this kind of data and we did not have access to direct observations. It

was possible to generalise to theory but further research is needed to evaluate the findings' applicability to other patients and settings.

Negotiations are linked to the role of power and ethical issues. Patients may perceive difficulty in communicating illness and powerlessness in attaining care. Providers have the difficult task of allocating resources based on assessments of illness and the optimal benefit of interventions. In negotiations, decisional conflicts and disagreements may arise that need to be resolved. There is a need to support both patients and providers in this complicated process.

Shared decision-making (SDM) has been suggested to enhance collaboration with psychiatric patients (Hamann et al., 2003). This is a challenge as 'brain diseases' affect patients' capacity to understand illness and to express needs, and as complexity of illness expressions can lead to misunderstandings. I suggest a model for shared understanding and treatment planning with dysthymic patients that may be applicable to other groups. The model stresses the centrality of interpersonal communication, the needs of integrating understanding of illness from the perspectives of patients and providers, and continuous follow-up to overcome the barriers for recognition and treatment. Health services need to develop supporting structures for re-evaluation and negotiation. Furthermore, I suggest that the life-charting methodology may be a diagnostic tool in assessing course, life events and evaluation of treatment, as well as a helpful tool for a collaborative relationship with the patient.

5.4 ON METHOD

The findings need to be interpreted with caution on account of selection (i.e. long illness duration, exclusion of comorbid dysthymia and panic disorder), the small sample size and the relatively low retention rate in the follow-up investigation. Other limitations are the risk of memory bias in retrospective data, and that the analysis of the interaction between patients and providers primarily was based on case records.

However, by combining quantitative and qualitative methods in practice research, a deeper understanding was attained of factors that help or hinder enduring remission for two significant psychiatric disorders. The participants were assessed as being representative of the diagnostic groups. A general model for recovery from dysthymia and panic disorder is suggested, which may be further investigated. As the diagnostic categories in the DSM system are overlapping, heterogeneous and changeable over time, research needs to use several methodologies and perspectives. The findings support evolving treatment models (e.g. exposure-based methods with an emphasis on altering responses to emotional arousal for panic disorder, combined treatment for dysthymia), and could help to refine future classifications, e.g. by examining the belief of rejection in relation to depressive personality disorder and dysthymia. By adhering to standards for qualitative and mixed methods research, criteria for trustworthiness were achieved (Morrow, 2005; Tashakkori & Teddlie, 1998). Besides the need for further research in other contexts, information about the research process and the context may enable the reader to evaluate the transferability of findings.

6 CONCLUSIONS

To conclude, the main findings and suggestions in this thesis are as follows:

- 1) Misdiagnosis and undertreatment hinder recovery. One contributing factor is that providers have difficulty in perceiving the complexity of illness expressions of patients with dysthymia and personality disorder.
- 2) It is necessary to perform careful assessments of all comorbid diagnoses.
- 3) The self-assessment questionnaire DIP-Q is a valid method for describing personality disorder. Caution is recommended for comorbid depression and context.
- 4) Comorbid personality disorder contributes to worse treatment outcome of dysthymia and panic disorder in ordinary psychiatric care. One reason may be that these patients have difficulty in getting response for their requests due to communication problems (difficulty negotiating), fear and distrust.
- 5) Providers' lack of structured follow-up is an obstacle to recovery.
- 6) Treatment ingredients that involve affect control strategies may contribute to recurrence of panic disorder.
- 7) Essential ingredients for recovery are suggested: An understanding of illness that facilitates more adaptive coping than avoidance, enhanced flexibility of thinking, as well as antidepressant medication and social support. A helpful relationship to the health care provider is a vehicle for this change.
- 8) Patients with dysthymia and panic disorder perceived different helping relationships to therapists and different central areas for change.
- 9) Early-onset dysthymia needs to be recognised and distinguished from secondary depressions, e.g. by noting cognitive core symptoms and examining age of onset.
- 10) To enhance collaboration, means of shared understanding and treatment planning are suggested, such as combining diagnostic assessments with attention to patients' perceptually bound understanding of illness, goals and treatment preferences, as well as systematic follow-up including re-evaluations. Life-charting may be a tool.

7 FUTURE RESEARCH

In prospective, long-term follow-up investigations, designs that are related to goals rather than to time ought to be tested. This could be done by examining persistence of remission among patients who have achieved the ingredients of the suggested model for recovery.

Research should examine the predictive validity of diagnostic criteria for dysthymia and depressive personality disorder for outcome, and how these disorders are related to other personality disorders, as well as the influence of the core belief of rejection and associated strategies of concealing.

The hypothesised specific effect of the alliance factor ‘bond’ for the outcome of early-onset dysthymia should be tested in randomised, controlled treatment studies.

Future research should also study effects of collaborative care interventions for patients with long-lasting illness that support patients and their health-care providers in optimal shared decision-making. Moreover, the issue of whether responses to interventions are influenced by patient characteristics needs to be elucidated.

8 SVENSK SAMMANFATTNING

Denna avhandling har inspirerats av kliniska erfarenheter som psykiater och psykoterapeut. Den kliniska vardagen kan vara frustrerande eftersom många patienter med depressions- och ångestillstånd har återfall eller kvarvarande besvär. Idag finns en ökad medvetenhet om att målet för behandling ska vara remission och inte bara kortsiktig minskning av symtom.

Två patientgrupper som anses vara mer svårbehandlade är patienter med dystymi, en långvarig depression med vanligen smygande och tidig debut (före 21 års ålder), och patienter med paniksyndrom som har agorafobi (torgskräck). Sådana patienter bör kunna förmedla viktig kunskap om förutsättning och hinder för återhämtning i vanlig psykiatrisk vård. Samsjuklig personlighetsstörning är en faktor som i många undersökningar visat sig ha negativ effekt på behandlingsresultat. Diagnosen personlighetsstörning avser tidigt debuterande varaktiga, omfattande och oflexibla mönster av uppfattningar och beteenden som avviker från personens sociokulturella sammanhang. Instrument som mäter kliniskt relevanta diagnoser har styrkor och begränsningar. De fångar inte unika individuella upplevelser. En genomgående tanke i denna avhandling är att klinisk forskning som kombinerar patientens och professionens perspektiv ger en mer fullständig bild av de fenomen som vi vill undersöka.

Syftet med avhandlingen är att öka kunskapen om faktorer som underlättar och hindrar varaktig remission (återhämtning) från dessa sjukdomar i vanlig psykiatrisk vård. Speciellt uppmärksammas hur sjukdomsförståelse hos patienter och vårdgivare kan påverka upptäckt, behandling och utfall.

I artikel I undersöktes validiteten (giltigheten) av DIP-Q, ett självskattningsinstrument för personlighetsstörningar enligt diagnossystemet DSM-IV, i tre kliniska grupper och en kontrollgrupp. Personlighetsprofiler mätta med DIP-Q kunde skilja mellan grupperna. Depression och att tillhöra en grupp psykoterapisökande visade ett signifikant oberoende samband med självskattad personlighetsstörning.

Artikel II och III redovisar resultat från en 9-årig prospektiv naturalistisk behandlingsstudie med antidepressiv medicin och psykoterapi av patienter med dystymi och paniksyndrom. I studien kombinerades kvantitativa och kvalitativa metoder.

I artikel II observerades låg frekvens av återhämtning bland patienter med lång sjukdomshistoria; ungefär 50% var förbättrade, varav 25% var återhämtade. En modifierad Life-charting metod användes. Tillsammans med genomgång av journaler tydde den på att underbehandling bidragit till sämre utfall. Samsjuklig personlighetsstörning var en negativ prognostisk faktor oberoende av symptomdiagnos. Patienter med paniksyndrom hade försämrats jämfört med utfallet efter två år.

Artikel III redovisar resultatet av kvalitativ innehållsanalys av djupinterintervjuer. Gemensamma faktorer som underlättat återhämtning var: sjukdomsförståelse som medfört bättre hanterande av obehag, mer flexibelt tänkande, tilltro till terapeut/vårdgivare, antidepressiv medicin, och socialt stöd. Det största gemensamma hindret till återhämtning var svårigheter att förhandla vård. Speciellt patienter med personlighetsstörningar hade problem med att uttrycka och få gehör för sina behov. Patienter med dystymi och paniksyndrom beskrev olika typer av hjälpsamt relation till terapeuten ('som en förälder' eller 'som en coach') och olika centrala områden för

förändring ('självacceptans och lösa relationsproblem' eller 'identifiera och hantera känslor').

I Artikel IV användes kognitiv utvecklingsteori som ramverk i en teoritestande och explorativ multipel fallstudie för att undersöka hinder till upptäckt och behandling av patienter med tidigt debuterande dystymi. Patienterna hade i regel beskrivit sin sjukdom mångfacetterat; med konkreta sinnesförnimmelser, metaforer, prototypiska upplevelser eller händelsekedjor. Detta stöder teorin att patienter med dystymi uttrycker sjukdomsförståelse med preoperationella kunskapsstrukturer enligt Piagets terminologi. Vårdgivarna hade huvudsakligen fokuserat på enstaka aspekter, vilket tolkades bero på selektiv uppmärksamhet. Andra hinder var att patienterna höll fasaden mot andra på grund av rädsla för avvisande och misstro, vårdgivarnas attityder, problem med tillgänglighet och att vårdgivarna inte följde upp behandlingsresultaten.

Sammanfattningsvis har resultaten från avhandlingen bland annat kunnat visa att:

- 1) Underdiagnostik och underbehandling är hinder för återhämtning. En bidragande orsak är att vårdgivarna har svårt att uppfatta den mångfacetterade sjukdomsbeskrivning som patienter med dystymi och personlighetsstörning förmedlar.
- 2) Självskattningsformuläret DIP-Q är en valid metod för att beskriva personlighetsstörningar.
- 3) Samsjuklig personlighetsstörning bidrar till sämre behandlingsutfall i vanlig psykiatrisk vård. En anledning kan vara att dessa patienter har svårt att få gehör för sina behov på grund av kommunikationsproblem (svårighet att förhandla), rädsla och misstro.
- 4) Ett hinder till återhämtning är brist på strukturerad uppföljning.
- 5) Viktiga ingredienser för återhämtning är bl.a. att patienten får en sjukdomsförståelse som gör att hon/han kan hantera obehag på ett mer adaptivt sätt, mer flexibelt tänkande, och en tillitsfull relation till terapeut/vårdgivare.

För att fler patienter ska kunna uppnå återhämtning och för att öka möjligheterna för alla vårdsökande att få optimal behandling, är det viktigt att diagnostisera samsjukliga tillstånd. Det är särskilt viktigt att även samsjuklig personlighetsstörning beaktas vid behandlingen.

Tidigt debuterande dystymi bör uppmärksammas och skiljas från sekundära depressioner, bl.a. genom att notera kognitiva kärnsymtom och rutinemässigt undersöka debutålder.

För att förbättra samarbete och kommunikation föreslås en modell för gemensam förståelse och behandlingsplanering mellan patient och vårdgivare.

I denna modell ingår bl.a. att kombinera diagnostiska bedömningar med uppmärksamhet på patientens konkreta sjukdomsförståelse, målsättningar och önskemål, samt att systematiskt följa upp med utvärderingar.

Life-charting metoden kan vara ett hjälpmedel.

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11 APPENDIX I – INDIVIDUAL-SPECIFIC SCALE

<p><u>Level 1. Life</u> <i>Happy, full of expectations.</i> <i>Self-confident.</i> <i>Finds possibilities.</i> <i>Curious, open, lively, spontaneous, engaged.</i> <i>Do things that make me feel good.</i> <i>My body is free and easy</i></p>	<p><u>Level 2. Vulnerable</u> <i>Happy, but easily disturbed.</i> <i>A bit restricted. Others perceive me as reserved.</i> <i>A little hope, but fragile.</i> <i>Low expectations of the future.</i> <i>I do know some things.</i> <i>Difficult to assert myself and my needs.</i> <i>Good worker.</i></p>
<p><u>Level 3. Boring - survive</u> <i>Inhibited, subdued, cautious.</i> <i>Less initiative.</i> <i>Fear of making mistakes.</i> <i>I'm not as good as others, I'm abnormal.</i> <i>Nobody wants me, I'm boring.</i> <i>My body is heavy and sluggish. My movements are restricted and stiff.</i> <i>Worry, tensions.</i> <i>Do what I need to do, avoid contact with others</i></p>	<p><u>Level 4. Isolation - hopelessness</u> <i>Feeling: I'm totally alone, not in contact with others.</i> <i>Disaster.</i> <i>Self-image "An UFO".</i> <i>Hopelessness, it cannot get better.</i> <i>Only exist, not live. Empty, in a shade, living dead.</i> <i>Suspicious. Difficulty in contacts with others, nothing to talk about.</i> <i>One should behave and do what one should do, but cannot.</i></p>

Figure 1. Example of an Individual-Specific Scale, Generated by a Woman with Dysthymia in Partial Remission to be used in the Modified Life-Charting Interview

12 APPENDIX II - CONTENT ANALYSIS

Table 5. Examples of Meaning units, Coding at Manifest and Latent levels, Subcategories and Categories from a Content Analysis of a Narrative of a Woman in Remission from Dysthymia for 4 years

Meaning units	Condensed meaning units Description close to the text	Condensed meaning units Interpretation of meaning	Subcategories	Categories
<i>Well, it started with that I met a woman who told me that I had very small chances of, or in fact no chances at all, I perceived that she told me that I shouldn't bother to apply because there were those who were more psychiatric, well more psychiatrically ill than I was.</i>	Assessor said I was not ill enough to get psychotherapy	Rejected request	Misunderstood and rejected	Difficult negotiations
<i>Ehh and so, but then I was also somewhat stubborn maybe, because I took contact again and after a while I was allowed to take my place in the queue and after quite a long time I was called to assessment.</i>	I was stubborn Allowed to take my place Long wait	Fought for request Asserted needs Critical of delay	Fought for my request	Difficult negotiations Successful negotiations
<i>(Describes a vivid and detailed autobiographical memory of the meeting with the assessor) I received what I wanted. I wanted to come back to my former therapist.</i>	Long wait, long wait in waiting room, angry, not functional to be angry, turns anger into crying Assessor turns to being like a mother, suggests medication. P rejects medication, expresses request	Aware of feelings Regulated feelings and context Knew and asserted request Received request	Problems financing psychotherapy Fought for my request Found finance for psychotherapy Chose my therapist	Difficult negotiations Successful negotiations Confidence in therapist

13 APPENDIX III - CONTENT ANALYSIS

Table 6. Examples of Meaning units, Coding at Manifest and Latent levels, Subcategories and Categories from a Content Analysis of a Narrative of a Man with Persistent Dysthymia

Meaning units	Condensed meaning units Description close to the text	Condensed meaning units Interpretation of meaning	Subcategories	Categories
I: What kind of expectations did you have? P: <i>Yes, to take away the most acute. What should I say the suicidal thoughts I had </i>	Wanted to get rid of suicidal thoughts	<i>Contradiction: Case records show several requests for "understanding" that were rejected</i> Low expectations	Misunderstood and rejected	Difficult negotiations
I: Did the medication help you? P: <i>Yes, a little. One could say that I didn't know..... how bad I felt. I didn't know, I didn't know the grade, and..... hmm.....</i> I: How do you view that although no medicine helped much, there was no other help? P: <i>Yees that one may have some sort of fear of medications, it was instinctively I dropped out</i>	Little help from medication Did not know my state Instinctive fear of medication Dropped out	Little help from medication Lack of awareness Fear of medication Difficulty asserting own needs	Medication stabilises Lack of awareness Fear of medication	Lack of understanding Fear of medication Difficult negotiations
I: You told me that you had felt ill for many years and that when you sought help 10 years ago you were allowed to try different kinds of antidepressant medications without much effect. And you have not sought help again despite not feeling well? P: <i>No, no, I don't think that I'm that bad.</i>	Not bad enough to seek help again	Difficulty communication Lack of awareness <i>These factors prevent help-seeking despite suffering and impairment</i>	Lack of understanding	Difficult negotiations Lack of understanding