CHAPTER 7

SUMMARY, DISCUSSION AND FUTURE PERSPECTIVES

7.1 Introduction

There are two approaches to psychopathology, a categorical and a dimensional approach. In the categorical approach each psychiatric disorder is characterized by a set of criteria. Diagnoses are made by checking whether a patient meets the criteria for one or more disorders. This is basically a dichotomous decision process; a patient meets criteria and therefore has a disorder or not. At first sight, this approach seems pretty straightforward for research and clinical practice. In etiological research it enables the study of well-defined patient groups. In clinical practice, the psychiatrist or therapist who made a diagnosis knows which treatments are appropriate, based on randomized controlled trials carried out in patients with the same disorder. However, patients with the same disorder may differ very much in symptomatology. For instance, if both patients have a depression (i.e. both have the required 5 out of 9 symptoms) they may have only a single symptom in common. Besides, in clinical practice comorbidity is the rule rather than the exception and this contributes to the heterogeneity. For research into the etiology of psychopathology this heterogeneity may explain why the results are often inconsistent. For clinical practice this implies that the evidence on which treatments are based is oversimplified. This may play a role in the often modest treatment results.

The dimensional view has the potential to overcome these problems as it allows a more comprehensive analysis of psychopathology. First of all, subjects are assessed not on a single, but on multiple dimensions. It is in fact a multidimensional approach. Each dimension is not assessed as present or absent, but is quantified along a continuum. And each patient is assessed along all the dimensions included in the investigation. The result is a much more refined profile of psychopathology than could be achieved with a categorical approach. For etiological research this may improve the chances to find a relationship between for instance biological factors and psychopathology. For clinical practice it allows (provided enough data are available) more refined choices for treatment and a better prediction of the prognosis.

The aim of this thesis was to investigate diagnostic heterogeneity and to test the feasibility of dimensional models in a large, real-life group of psychiatric outpatients with mood, anxiety and / or somatoform disorders and to develop a dimensional model that overcomes the disadvantages of existing ones. Before discussing the results, the major findings will be summarized.

7.2 Summary of major findings

As the data of all patient samples in this thesis were collected with Routine Outcome Monitoring (ROM), we first described this method in detail in Chapter 2. Although they initially had their reservations, most therapists considered ROM to be an important adjunct to diagnostics and treatment outcome evaluation. In addition, ROM furthers research as the data can be used to study

the phenomenology of psychiatric disorders and the outcome of treatments delivered in everyday practice. Implementation of ROM in outpatients with depressive, anxiety and somatoform disorders therefore seems to be feasible and useful.

Next, we investigated whether in this patient sample a high rate of comorbidity (as discussed in 7.1) could indeed be found. We analysed the prevalence of axis 1 DSM-IV disorders in a group of 3798 outpatients who had had ROM-assessments. According to the MINI-Plus (part of ROM), 1,618 patients (42.6%) met criteria for a single mood, anxiety, or somatoform (MAS) disorder, but nearly the same number, 1,556 patients (41.0%), had more than one concurrent MAS disorder: 967 patients (25.5%) had two comorbid disorders, 403 patients (10.6%) had three, and 186 patients (4.9%) had four or more. This high prevalence of different types of comorbidity signifies heterogeneity.

In Chapter 3 we examined whether the comorbidity discussed in Chapter 2 is merely the coming together of two or more disorders in the same patient or whether the whole is more than the sum of its parts. To do so, we compared the scores of patient groups defined by the categorical diagnoses on several severity assessments, This approach is 'semi-dimensional' as it stays close to the diagnostic categories but allows quantification. We found that depression severity in the comorbid group was higher than in the pure depression group and that anxiety severity in the comorbid group was higher than in the pure anxiety group. This study also revealed that the mean scores on the anxiety measures did not differ significantly between patients with a pure depression and patients with a pure anxiety disorder. These results show that, with respect to symptom severity, comorbidity is more than simply the sum of the disorders.

We also wanted to go beyond categorical diagnoses and explore a more fully dimensional model with dimensions not necessarily coupled to the diagnostic categories of depressive and anxiety disorders. We chose an already existing model as point of departure: the tripartite model of Watson and Clark. This model proposes that there is one nonspecific general distress factor (negative affect), common to both mood and anxiety disorders, and two additional factors specific to anxiety disorders and depression. The three dimensions of the tripartite model can be measured with the MASQ (Mood and Anxiety Symptom Questionnaire). In order to do research on the tripartite model in Dutch samples, a translation of the MASQ was needed. In Chapter 4 the Dutch adaptation of the MASQ is presented and the applicability of the tripartite model on our sample is tested. The psychometric properties of the translated MASQ were highly satisfactory. In accordance with the model, we found the MASQ to comprise three main scales, which discriminate well between subgroups of patients with mood and anxiety disorders.

Although the tripartite model has inspired a large body of research, it has met some criticism as well. A major point of critique is that depression is well

covered with lack of positive affect and negative affect (a nonspecific aspect of the disorder). However, the same cannot be said for anxiety, as the dimension 'somatic arousal' that is specific for anxiety does not cover all anxiety disorders but mainly covers panic disorder. Somatic arousal is too narrow as a conceptualization of anxiety, ignoring other important aspects of anxiety such as anxious apprehension, worry, phobic anxiety and/or avoidance.

In Chapter 5, we present a first model that contains clearly distinguishable constructs, and includes main aspects of common mental disorders in outpatients. Our aim was to cover anxiety more adequately than the tripartite model does. We used items of the Mood and Anxiety Symptom Questionnaire (Watson & Clark, 1991) and items of the Brief Symptom Inventory (Derogatis, 1975). A model with five dimensions was found: depressed mood, lack of positive affect, somatic arousal, phobic fear and hostility. The validity of the model was supported by the following findings: The scales appeared capable to differentiate between patients with either a mood or an anxiety disorder. Low positive affect and phobic fear were the best discriminators between depressed patients and patients with an anxiety disorder. Within the anxiety disorders, somatic arousal was specific for patients with panic disorder. Phobic fear was associated with panic disorder, simple phobia and social anxiety disorder, but not with generalized anxiety disorder.

Whereas the study described in Chapter 5 validated the model by comparing the dimensions to the categories of the DSM-IV (disorder-based approach), in Chapter 6 we took a step further away from the DSM-IV and closer towards a 'true dimensional model' (symptom-based approach). As point of departure we used a large item-pool that included (1.) the items of the Mood and Anxiety Symptom Questionnaire (Watson & Clark, 1991) to measure NA, PA and SA, (2.) items of the anxiety subscales of the Brief Symptom Inventory (Derogatis, 1975), to measure fearfulness and (3.) newly designed items to measure anxious apprehension. By using two different patient samples to develop and evaluate this second model, we arrived at a 6-factor model: feelings of worthlessness, fatigue, somatic arousal, anxious apprehension, phobic fear and tension. Somatic arousal, anxious apprehension and phobic fear are all clearly anxiety-like constructs. Thus, instead of only the single anxiety dimension of the tripartite model (somatic arousal), the present model distinguishes three groups of symptoms. Each individual factor and the total of factors can be regarded as unidimensional measurement scales, and this model can describe the clinical state of patients more specifically than the tripartite model.

7.3 Discussion

7.3.1 The results

The studies presented in this thesis are explorations along the road to a fully dimensional model of psychopathology. Below we will discuss what we contributed and what our contributions mean.

First of all, we showed in our own sample of secondary care outpatients with depression, anxiety and somatoform disorders that comorbidity is highly prevalent. This is in line with the findings of an extensive body of literature on comorbidity. High rates of comorbidity between anxiety disorders and depression have also been reported in the general population (Kessler et al., 1996), in primary care (Roca et al., 2009) and in secondary care (Brown et al., 2001). In fact, comorbidity of depressive and anxiety disorders is so prevalent that it is no coincidence (Kessler et al., 1996). These findings launched research into the existence of psychopathological dimensions common to anxiety and depression (Clark & Watson, 1991) and into genetic overlap (Kendler, 1996). The psychopathological dimensions common to depression and anxiety disorders will be discussed later, after the role of the dimensional approach in assessing the severity of comorbid disorders. The possible genetic overlap goes beyond the scope of this paper and will not be discussed further.

We showed that in depression and anxiety disorders comorbidity is more than simply the sum of diagnoses. For instance, we found that some symptoms of comorbid occurring disorders, are more severe than if the disorders occur alone. This has also been reported in other studies (e.g. Dalrymple & Zimmerman, 2007; Fava et al., 2004; Kaufman & Charney, 2000) but has never been studied for comorbid depression and anxiety disorders and single depression and single anxiety disorders in the same clinical sample. Together with the symptom heterogeneity possible in patients with the same diagnosis (see 7.1), the results suggest that the categorical diagnoses as defined in the DSM-IV are too indistinct. Assessing symptom severity may make etiological research more fruitful and may also help to find more effective treatments. We will discuss this more comprehensively further on. For now, it suffices to say that the proposal to include the assessment of symptom severity in the DSM-5 signifies growing support for this view.

What is the best instrument to assess dimensions of depressive and anxiety symptoms? In fact, every multi-item questionnaire on depressive and / or anxiety symptoms yields a quantitative assessment of one or more aspects of psychopathology and thus may qualify for the assessment of these dimensions. We chose the Mood- and Anxiety Symptom Questionnaire (MASQ) of Watson and Clark (1991) as it is based on their tripartite model. The significance of this model lies in the fact that it tries to take into account the overlap as well as the diversity in psychopathology in subjects suffering from depressive and / or anxiety disorders. The overlap is assessed with a non-specific distress factor

(negative effect) and the diversity with a factor specific for depression and one for anxiety. The MASQ also was chosen because of its use in many studies, also with respect to etiology, not only with adult patients (Marshall et al., 2003; Joiner et al., 1999; Keogh & Reidy, 2000) but also in child psychiatry populations (Chorpita & Daleiden, 2002).

As we made the MASQ the central assessment tool of our further investigations, it was important to have at our disposal a translated and psychometrically sound Dutch version. We carefully translated the MASQ and demonstrated good reliability and validity of this Dutch version in a large sample of 950 outpatients referred to secondary care because of mood, anxiety and/or somatoform (MAS-) disorders and 200 respondents from the general population. We did not include inpatients, primary care patients and patients with other disorders as our research focused on outpatients with MAS-disorders. However, in the future the MASQ should also be evaluated psychometrically in those groups of subjects. The present analysis showed that the factor structure of the MASQ with three factors was preserved in the Dutch translation. Factor-loadings of items and allocation of items to subscales was similar to results of Watson and Clark with US clinical samples and with patient samples from Great Britain (Keogh & Reidy, 2000). Recently, our group has developed and evaluated a shortened 30-item version, called the MASQ-D30, thereby increasing the feasibility of its incorporation in an assessment battery for ROM (Wardenaar et al., 2010).

Translation of the MASQ was not the primary aim of our study, but rather a means to an end. Our main aim was to remediate the shortcomings of the tripartite model and the MASQ. The original authors recommended already in 1998 to view in future research "individual disorders as representing unique *combinations* of different types of symptoms, with each type showing varying degrees of nonspecificity and with no type being entirely unique to any single disorder" (Mineka et al., 1998, p.398). We operationalized this idea, by developing symptom scales that include the more unique symptoms of specific mood and anxiety disorders in addition to common symptom scales. As described in chapter 5, by adding items of the BSI to the MASQ the new questionnaire was able to distinguish three groups of symptoms, each one specific to a different kind of anxiety disorder (panic disorder, GAD, and phobic disorders) instead of only the single anxiety dimension of the tripartite model (somatic arousal).

However, remediating the shortcomings of the MASQ in differentiating between the various DSM-IV categories of mood and anxiety disorders was not our final goal either. Rather, we set out to develop a broad dimensional model, not taking DSM-IV diagnoses as a point of departure nor taking specificity to particular DSM-IV diagnoses as the best sign of validity. We aimed for a multidimensional model to characterize individual patients in

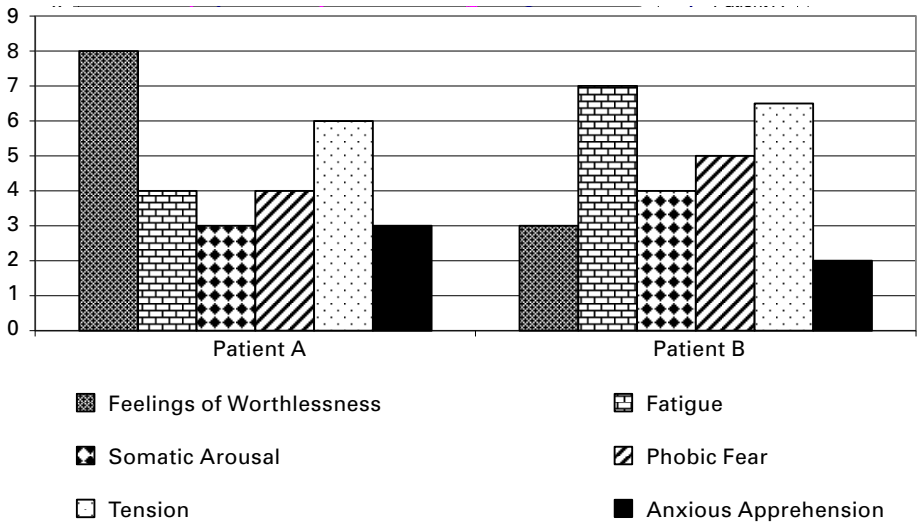

Figure 7.1 Fictional example of a 'symptom profile' for two patients, both diagnosed with Major Depressive Disorder according to the DSM-IV.

terms of their specific symptom profile by including extra symptoms to a self-report instrument in order to cover additional dimensions. As described in chapter 6, this resulted in a 6-factor model: feelings of worthlessness, fatigue, somatic arousal, anxious apprehension, phobic fear and tension. This model reveals differences in symptom profiles between patients who, according to the DSM-IV would all have been diagnosed with MDD. Figure 7.1 gives a graphic representation of the symptom profile of the two exemplary patients we introduced in the introduction of this thesis. Not only patients with MDD, but also patients with anxiety disorders and patients with comorbid depression and anxiety, can be characterized with the same 6 factors.

The dimensions may be a fruitful basis for future research into prognostic factors of treatment response. It may well be that an optimal match exists between symptom profiles and treatment modality. By assessing large groups of patients before and after treatment with, for instance, selective serotonin reuptake inhibitors (SSRIs), it will become possible to determine which profile(s) are most sensitive for these drugs. Finding the most appropriate treatment (pharmacologically or psychotherapeutic) can be a lengthy trial-and-error process. Matching of patient characteristics to treatments is the next step in improving evidence based medicine in psychiatry (Beutler, Forrester, Gallagher-Thomson, Thompson, & Tomlins, 2012). Eventually, this information

will help to address the famous question first raised by Gordon Paul: "what treatment, by whom, is most effective for this individual with that specific problem, and under which set of circumstances?" (Paul, 1967, p.111).

The model presented in Chapter 6 is a hierarchical model with a bifactor structure (see for a graphic representation: model 5 in Figure 6.1). Confirmatory factor analyses showed that this bifactor hierarchical model with a general severity factor and six specific factors fitted best to the data, compared to several other models. In a hierarchical bifactor model, different sets of items loaded on specific factors and, at the same time, all items loaded on one general severity factor. With a hierarchical common factor it is possible to determine severity and to differentiate between non-patients and patients. The dimensions can be used to form a unique symptom profile for each patient to differentiate within patients.

The tripartite model is a unifactorial model with 3 factors. In a unifactorial model a set of items load on one factor (see for examples of unifactorial models: model 1, 2 and 3 in Figure 6.1). An important feature of the tripartite model (Clark & Watson, 1991) is the difference that is made between general and specific distress. The factor negative affect in the model is presented as general distress, whereas 'lack of positive affect' and 'somatic arousal' are presented as dimensions of distress specific for respectively depression and anxiety disorders.

This difference in general and specific distress is also an element in several other models which were previously suggested as reaction to the critiques on the tripartite model (Brown et al., 1998; Mineka et al., 1998; Zinbarg & Barlow, 1996). There is consensus that both general and specific components are needed to fully represent the variation observed among mood and anxiety disorders (Simms et al., 2008). It is confusing, however, that the terms 'general' and 'specific' are not used consistently in literature. They can be used to refer to the content of a factor, and also to refer to their place in a higher-order or hierarchical model. For example, NA in the tripartite model is not a general factor according to the methodological structure of the model (a unifactorial model does not contain any general, higher order or common factor). However the content of NA is general (since it represents general distress and not a specific symptom), and in this context the term *specific* means specific to a (group of) disorder(s) or patients. We advocate to refer to NA as non-specific, and to avoid the term general in this context. In a hierarchical, bifactor model, we prefer to speak of unique and common factors.

We concluded that a hierarchical 6-factor model is optimal to describe the structure of the symptom dimensions of mood- and anxiety disorders, when integrating important aspects of the tripartite model and the valence arousal model. As suggested by Mineka et al.(1998), the six unique factors in our model describe a patients' symptom-profile, while at the same time the complete set of items reflects overall severity. Importantly, our findings are in line with earlier

studies (Simms et al., 2008; Simms et al., 2012) and lend further support to the idea that the symptomatology of depression and anxiety has a hierarchical structure.

7.3.2 Limitations

The results should be interpreted in the light of some limitations. First, we took the symptoms mentioned in the DSM definitions of mood and anxiety disorders as a starting point. In theory, other symptom dimensions could be of importance to describe the phenotype of mental disfunction which show different associations with etiology, the course and treatment of mental problems. However, depressivity and anxiety are universal notions that are elaborated by psychology and psychiatry. Positive and negative affect, the two dimensions from the circumplex model of affect (Watson & Tellegen, 1985) that Watson and Clark used in their tripartite model (Clark & Watson, 1991), are also strongly embedded and universal (Russell & Lewicka, 1989).

Second, the described studies are limited to the common mental disorders depression and anxiety disorders (both internalizing disorders). Although the difference between internalizing and externalizing disorders is often confirmed in research (Kessler et al., 2005; Kotov et al., 2011; Vollebergh et al., 2001), symptoms of externalizing disorders are also present in patients with internalizing disorders (and vice versa). For example, Koh and colleagues (2002) found a predominance of anger in depressive disorders compared with anxiety disorders and somatoform disorders. Therefore, it is worthwhile to extend the model with externalizing dimensions (Krueger et al., 2005) comprising concepts such as 'anger' or 'aggression' (Pasquini et al., 2004; Picardi et al., 2004). We made a start with the dimension 'hostility' in the model presented in Chapter 5.

Third, the results only apply to outpatients before the start of their treatment. This implies that the findings cannot be generalized to inpatients or to persons with "normal" or nonpathological levels of anxiety and depression as a general model of affect. To make a model that can be generalized to the normal population it might be useful to measure all dimensions with both negatively and positively formulated items. After all, the measurement range of the dimensions will be wider when positively formulated items are included as well.

Fourth, the results only apply to patients with specific demographic characteristics. Approximately 80 percent of the patients in our samples were born in The Netherlands, as were both their parents. On top of that, a condition to participate in ROM was to master the Dutch language well, both spoken en written. Therefore, no statements can be made about to what extent our results apply to patients with different ethnic backgrounds or literacy. Moreover, the results cannot be generalized to children and elderly, since we used patient samples of adults only.

Finally, this thesis focused on the reliability and the internal validity of the multidimensional models, not on the external validity. We did not investigate to what extent the dimensions correlate with biological factors like cortisol levels or polymorphisms and to what extent they predict treatment success and the course of the mental problems. This was done, but as yet with the original dimensions of the MASQ, by other members of the research group of the LUMC department of psychiatry. Van Veen et al. (2013) found that childhood traumas have different effects on the MASQ dimensions, whereas most adult life events are associated with all three. Wardenaar et al. (2012) showed that MASQ dimensions predicted the future 2-year course of depression and anxiety. Importantly, the dimensions yield predictive information on top of DSM-IV diagnoses. Luppino et al. (2011) demonstrated a strong association of most components of the metabolic syndrome with the SA dimension, but not the PA and NA dimension of the MASQ. Veen et al. (2011) and Wardenaar et al (2011) both found non-linear relations between the cortisol awakening rise (CAR) and dimensions of the MASQ, which could explain previous inconsistent findings regarding HPA-axis activity in depressed patients. And last but not least, Veen et al. (2012) showed that MASQ-dimensions were each associated with specific gene sets. It can be concluded that the external validity of the original MASQ dimensions is promising. It will be interesting to investigate the external validity of the extended dimensional model presented in this thesis.

7.3.3 Future perspectives

Before adopting a dimensional approach on a large scale, the superiority of the dimensional approach to the DSM-IV for the characterization of patients, the investigation of the etiology and the clinical utility needs to be demonstrated (First, 2005). Future research has to show whether a dimensional profile is indeed useful in deciding what the main target for treatment should be and what kind of treatment is indicated. For example, an overactive sympathic nervous system as revealed by high anxious arousal may require a different pharmacotherapeutic approach, while a high propensity to worry may suggest psychosocial therapy. With the original scales of the tripartite model, the first progress in using dimensions in research into etiology is already made. For example, Wardenaar found nonlinear associations between characteristics of the stress-system (cortisol awakening curve) and the dimensions of the tripartite model (2011) in a sample of outpatients.

In most current research into the etiology of common mental disorders, patients are compared to controls regarding the presence of specific genes, or other biological or psychological variables. Most commonly, this is done with a categorical "mindset": the presence or absence of a trait or biological marker is investigated in persons with or without a diagnosis (e.g., patients with a major depressive disorder as compared to controls). A dimensional model

however requires a correlational "mind set": etiological factors (themselves often measured on a continuous scale) may be strongly correlated with some (combinations of) dimensions and less strongly with others, irrespective of the categorical diagnoses the patients have. Thus, in research aimed for instance at the endophenotypes of psychopathology we might find the "anxious apprehension profile" rather than "anxiety disorder". It is quite a challenge for researchers to switch from a categorical to a correlational mind set. After all, all humans have a strong tendency toward categorization as we are more inclined to separate and sort things (safe - unsafe, edible - not edible) so we know how to navigate in the world around us. This 'mental categorization' is one of the first stages in our cognitive development, and starts at a very young age (Piaget, 1962). Besides our early learned custom to think in categories, another difficulty is that dimensions are much more complex to depict than categories, especially when more than 3 dimensions are involved.

A pleasant consequence of using multi dimensional models in research is that statistical power is usually substantially enhanced if true variance in affect scores is assessed and preserved in the analysis. This is easily demonstrated by comparing a dimensional depression score with the dichotomous categorization of depressed vs. non-depressed. With the latter, much information is sacrificed which would have been preserved in the former.

On the other hand, using dimensions in research means that the required statistical methods are more complex than when using categories. A t-test between two groups (e.g. not depressed vs. depressed) to test for a significant difference on another variable won't do. Multiple regression analyses with special attention for interaction effects will be necessary. Fortunately, these techniques are now available in statistical software.

It is preferable that all symptom dimensions are analysed simultaneously. Although the correlations between the dimensions are relatively low, they are correlated. If one would study or analyse them one by one, correction for this correlation is not possible and the wrong conclusions might be drawn. For example the conclusion might be drawn that a specific treatment does not have an effect on both dimensions A and B separately, while the interaction effect is missed.

A more general point about the use of dimensions in research is that they break with the simple tradition of comparing etiological factors between healthy and diseased groups. This can lead to a disruption in research efforts; e.g. combined meta-analyses are not possible on studies that use DSM-categories and studies that use a dimensional approach. This drawback can be prevented by a combined approach (using both the DSM and dimensional measures). For research, a combined approach has great benefits over using the categorical system solely (Brown & Barlow, 2005). It is already seen more and more in research that although the selection of patients for a research group

is still determined by the DSM-criteria, dimensional measures are added to the research design. An important advantage of this development is that individual differences between patients within one DSM-category are acknowledged (e.g. in analyses of experimental findings the scores on the dimensional measures can be taken into account as covariates). As Kaufman and Charney concluded: 'the use of categorical diagnostic approaches and dimensional rating scale in tandem will facilitate identification of meaningful phenotypes for future genetic, biochemical, neuroimaging, and treatment studies' (pag.73, Kaufman & Charney, 2000).

For the successor of the DSM-IV, the DSM-5 (published in May, 2013) it was suggested to combine categories with dimensional measures. The DSM-5 Work Groups were considering an additional way to help the clinician capture the symptoms and severity of mental illnesses, by using dimensional assessments. These would allow clinicians to systematically evaluate patients on the full range of symptoms they may be experiencing. For instance, information about depressed mood, anxiety level, quality of sleep, and substance use would be important for clinicians to know regardless of the patient's diagnosis. Dimensional assessments would allow clinicians to rate both the presence and the severity of the symptoms, such as "very severe," "severe," "moderate", "mild", or "absent". It would encourage mental health professionals to document all of a patient's symptoms and not just those that were tied to their primary diagnosis.

Adopting dimensions in the DSM-5 holds much promise. It is a start to advocate dimensions in the field. And, although clinical utility in the sense that assessed dimensions can be used to decide which treatment is most effective for a specific patient is not available yet, there is however already a benefit for the clinician in assessing dimensional measures next to the DSM-categories. When using both a diagnostic interview and several dimensional (severity) measures at intake, the clinician gets useful insights into the symptoms profile of each patient at intake and at follow-up (ROM), and therewith into the effect of the chosen treatment on different sorts of symptoms for the patient at hand.

We suggest using the same dimensional measures within all DSM-categories of common mental disorders. For example, only when anxiety is measured dimensionally in both patients with a depression as well as those with an anxiety disorder, analyses can be done in all categories simultaneously. Only then, research can be done without the restrictions of the DSM. ROM as implemented in 2002 in Leiden, proved to be a very useful instrument to measure dimensions and categories, and combined with biological data enhance our insight in the complex relationship between depression and anxiety and their common and distinctive etiological factors.

The multi-dimensional models presented in this thesis are limited to symptoms that were present at the time of the assessment. The questionnaires

used, ask the patient to report the level of presence of each symptom in the week prior to the assessment. A symptom profile generated with the models therefore does not contain any information about the history of the patient (duration, recurrence, familiarity etcetera). Determining what phase of the clinical course of the disorder a patients is in (staging) is very important. A clinical staging model, already widely used in oncology, could improve the utility of diagnostic characterisation in psychiatry as well, with emerging disorders (McGorry et al., 2007). Staging models are based on the fact that response to treatment is generally better when it is introduced early in the course of the illness. It assumes that earlier stages have better prognosis and require simpler therapeutic regimens (Vieta, Reinares, & Rosa, 2011). It would be ideal to include symptom-profiles ('profiling') in 'staging'. Routine Outcome Monitoring is an important instrument for developing staging and profiling in psychiatry (Zitman, 2012).

We believe that the main focus for the next years should be on research on profiling and staging with the aim to determine those factors that predict the evolution of symptoms and the effective treatment. This kind of research has the best chance of being successful when various research groups cooperate and find consensus about research designs and variables used and how to conceptualize them optimally. A dimensional approach to psychopathology is expected to be more successful than the traditional categorical approach, as it is a far better representation of the richness of clinical phenomena.