Treatment quality in times of ROM

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Chapter 1

General introduction and thesis outline

Introduction

In secondary mental health care the majority of patients are being treated for mood-, anxiety and/or somatoform (MAS) disorders. Evidence based guidelines have been implemented in clinical practice with the aim to optimize the pharmacological and psychological treatment of patients with these disorders. However, data on outcome of treatment and adherence to these guidelines in routine clinical practice are scarce. There is also limited data available on patient and therapist factors influencing adherence to guidelines for MAS disorders. Research into these topics is hampered by the lack of reliable, valid and easy to use tools to assess adherence to guidelines in clinical practice.

Mood-, Anxiety and Somatoform Disorders.

By far the largest group of outpatients in secondary mental health care are people suffering from Mood-, Anxiety- and/or Somatoform (MAS) disorders.
MAS disorders are responsible for a considerable burden of disease, as has been shown on several indicators [1].
MAS disorders show a high rate of comorbidity, which may be due to a shared etiology as well as to partially overlapping symptoms and vague diagnostic boundaries. Nevertheless, for each of these disorders separate treatment guidelines have been developed. Also, in patients treated for a single disorder, predictors of treatment response have been studied. In general it became clear that patients suffering from single MAS disorders often have a poor treatment response, with more than half of all patients failing to achieve remission after first-line treatment [2-5]. Longitudinal studies on patients treated for single mood-, anxiety, or somatoform disorders have identified several predictors for treatment non-response, irrespective of guideline adherence. In general, poorer remission rates in depressive disorders were predicted by being unmarried [6-8], being unemployed [8,9], a lower level of education [10], a greater severity of depressive symptoms [9,11], concomitant symptoms of pain, comorbid anxiety disorders [7,11-13], and borderline personality disorder [12,14]. Poorer remission rates from anxiety disorders were predicted by a higher severity of the anxiety symptoms, concomitant symptoms of pain, comorbid depression [13] and prevalent personality disorders [15,16]. Predictors of low remission rates

for somatoform disorders were a lower level of education, [10]concomitant symptoms of depression [17], a greater severity of the somatoform symptoms, and suffering from a comorbid personality disorder [18]. Although these data suggest the importance of comorbidity, comparable data on patients with comorbid MAS disorders are generally lacking.

In the treatment of MAS Disorders in clinical practice, the problem of comorbidity is solved in a pragmatic way: one of the disorders is designated as the main disorder and subsequently treatment is focused on that disorder, based on the guidelines for that disorder. As treatment options for MAS disorders are often overlapping, the chosen treatment for the 'main' disorder is often thought to be beneficial for the comorbid disorder(s) as well. However, evidence for this statement is scarce. Given the overlap of MAS disorders in symptoms, etiology and treatment options in clinical practice, it may be more informative for clinical practice to study these disorders not separately but as a group.

Guidelines

General

Clinical practice guidelines have been defined by the Institute of Medicine as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" [19]. Guidelines are thought to increase treatment quality and reduce costs. By translating the best available evidence into specific recommendations, guidelines can serve as useful tools to achieve effective and efficient patient care. Whereas guidelines initially were based on consensus among experts, guideline development has been formalized and evidence-based guidelines are the standard nowadays.

The first initiative to develop guidelines came from the National Institute of Health (NIH) in the United States in 1977 and consisted of a consensus document on the screening of breast cancer. Since that time, clinical guidelines are developed by medical societies and supported by special institutes, such as the National Institutes of Health (NIH) in the United States, the National Institute for Clinical Excellence (NICE) in England and by the Stichting Kwaliteitsinstituut voor de Gezondheidszorg of the Centraal Begeleidings Orgaan (CBO) in the

Netherlands. Developing evidence-based guidelines as such, however, does not guarantee improved quality of care.
They should also be implemented and effective implementation should ensure guideline adherence in practice and subsequently lead to improved patient outcomes. We will now discuss the development and implementation of guidelines in more detail.

Development

In general, a guideline is developed by a representative and respected group of experts from relevant professional organizations and patients, reaching agreement on the specific area of healthcare. Consensus is based on a systematic review of the available literature. Authorities like the Agency for Health Research and Quality, AHCPR/AHRQ for example, developed a system to estimate the level of the available evidence in the literature and use this to grade the recommendations for specific treatment in guidelines. In general, evidence derived from meta-analyses of randomized controlled trials is considered to be the most robust, followed by evidence derived from single RCTs, evidence from controlled studies without randomization, evidence from non-experimental studies (such as case-control) and finally expert (committee) opinions [20].
If no evidence can be found, an interview of experienced care providers can be performed, as is done in the Rand-modified Delphi Procedure [21], to quantitate 'expert opinion', in order to reach consensus about what is called the 'best practice'. The Appraisal of Guidelines Research and Evaluation (AGREE) instrument is an internationally acknowledged instrument to appraise guidelines and to select the appropriate guideline for a local setting [22].

Implementation

Effective implementation of evidence-based guidelines in routine care requires a multifaceted and systematic approach. Implementation programs should be built into the normal channels and structures for improving care [22-25].
Not surprisingly, an international survey of 18 clinical guideline programs in the United States, Canada, Australia, New Zealand, and nine European countries revealed that implementation strategies vary among different organizations and countries, with larger organizations leaving this to local organizations. Almost all initiatives had some kind of a quality assurance system for their

guideline development programs, with several submitting their guidelines to a guideline clearing house. Differences existed in the emphasis on dissemination and implementation, probably due to differences in health care systems and political and cultural factors [26].

Guidelines in the Netherlands

Inspired by the National Institutes of Health in the United States, the Netherlands the Institute for Healthcare Improvement (CBO) was established in 1979. The aim is to promote peer evaluation and to develop guidelines based on professional consensus. Guideline development has become a priority in the Netherlands since the late 1980's. The Committee Dekker (1987) gave the impetus for integrated care management, in order to reduce the massive expenses and to create more cohesion and transparency in health care. Guideline development and implementation was considered an important tool to ensure a more coherent medical decision-making process in health care [27]. In line with the advice of the Committee Dekker the Dutch College of General Practitioners (NHG) and the Dutch Society for Psychiatry (NVvP) formulated evidence-based guidelines for the treatment of several psychiatric disorders. However, both organizations developed their own guidelines. An example is the practical guideline for anxiety disorders in 1997 (NHG) and the guideline for the pharmacological treatment of anxiety disorders in 1998 (NVvP). These monodisciplinary guidelines were often limited to one specific treatment option, whereas in psychiatric practice several treatment options are available and often more than one discipline participates in the treatment process. Therefore, in 1999 the Dutch National Steering Committee for Multidisciplinary Guideline Development in Mental Health was founded to develop multidisciplinary guidelines in cooperation with the Dutch College of General Practitioners, the Dutch Society for Psychiatry and patient associations, supported by the Trimbos-institute (Netherlands Institute for Mental Health and Addiction) and the CBO. In 2003 the first multidisciplinary guideline for the treatment of anxiety disorders was published, followed by the multidisciplinary guideline for the treatment of depressive disorders in 2005.

For anxiety and depressive disorders, as well as for other psychiatric disorders, several treatment modalities are available. In the guidelines it is proposed to apply these treatments in a fixed order, according to a stepped-care model. However, research on the optimal order in which to apply these treatments

to obtain maximum treatment efficacy is still limited. Therefore, the order of the treatment steps is usually based on other principles: what is most feasible, less costly to apply and more tolerable by patients comes first. Figure 1 shows the steps in the treatment of major depressive disorder as an example of the stepped-care approach.

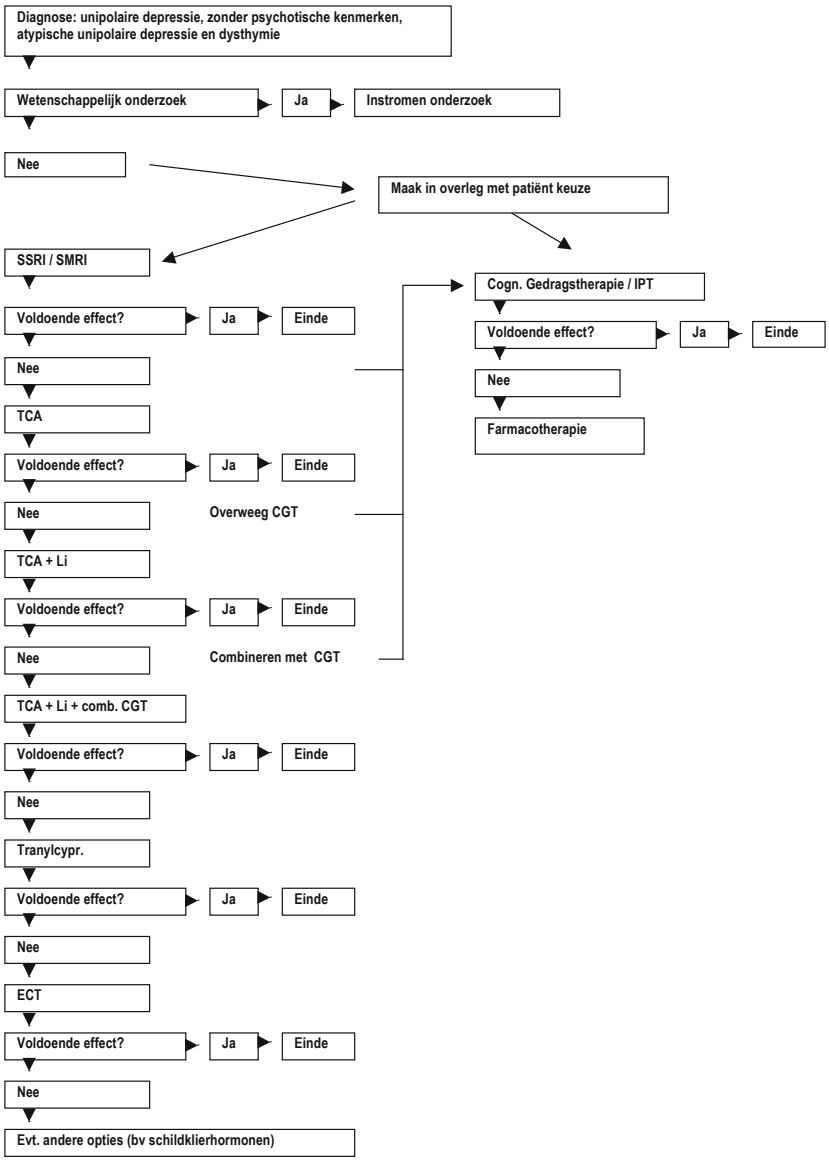


Figure 1: Guideline for mood disorders. GGZ Rivierduinen

Implementation in the Netherlands

The Dutch organization for health research and development (ZonMw) defined the process of implementation as "the planned and process-orientated introduction of innovations and/or changes of proven value, in order to become part of the functioning of an organization or part of the mental health care structure" [28]. These definitions have a rather theoretical character and raise curiosity about the actual implementation.

In the Netherlands guidelines are often integrated in more extensive programs of care developed by mental health providers, which are defined as "a set of agreements on care to a well-defined target group, resulting in a common framework for organizations, professionals and patients" [29]. These programs also "provide coherent care-options for the target group and not only describe which care at which moment should be applied, but also how the specific care has to be provided". For example: by which type of therapist, in which setting and how often"[30]. Up to now, these aspects of the implementation process in clinical practice has not been studied.

Adherence to guidelines

The effects of guidelines on treatment outcome in trials

Guidelines were introduced with the expectation that they would improve treatment outcome and reduce costs. Therefore, after the introduction of guidelines some studies were carried out to compare the outcomes of guideline-based treatments with treatment as usual. In 1990 the German Berlin Algorithm Project started. It compared the effectiveness and feasibility of a standardized stepwise drug treatment regimen (SSTR) for the treatment of inpatients with depressive disorders with treatment as usual [31]. The results of this project indicate that treatment algorithms increase the efficacy of applied treatments in the care of depressed patients. Remission rates and treatment outcomes were increased during the maintenance treatment phase [31].

In 1997 an American equivalent, the Texas Medication Algorithm Project, started. This was an effectiveness, intent-to-treat, prospective trial, comparing clinical and economic outcomes of an algorithm-driven disease management program (ALGO) with treatment-as-usual (TAU) for adults with DSM-IV schizophrenia, bipolar disorder and major depressive disorder treated in public

mental health outpatient clinics in Texas. The participating ALGO and TAU Clinics were prematched based on sociodemographic and clinical characteristics of their patient populations[32]. Evaluable patients were post-matched based on symptoms and length of illness.

ALGO consisted of a medication algorithm and manual to guide treatment decisions. Physicians and clinical coordinators received training and expert consultation throughout the project. ALGO also provided a disorder-specific patient and family education package. Quarterly outcome evaluations from ALGO and TAU patients were obtained by research coordinators, not blind to treatment assignment but not involved in providing any treatment. The outcomes of guideline-based treatment in ALGO patients were substantially better than treatment as usual.

The well-known seven year Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial in the United States was finished in 2006 and compared different treatment strategies in treatment-resistant patients by optimizing dose and duration of medication by a measurement-based care (MBC) approach, allowing patients with a wide range of comorbid general medical and psychiatric disorders in the trial, reflecting to a large extent a 'real world' approach. On the basis of the first treatment step with citalopram, over 85% of treatment encounters had appropriate fidelity to recommendations. Most deviations from treatment recommendations occurred late in treatment and were often justifiable [33]. The study provided evidence of the value of a MBC-approach, as it seemed to enhance vigorous but safe dose escalation in STAR*D and improve treatment results [34].

Adherence to guidelines in trials

The studies discussed above suggest that applying guidelines does improve outcomes, also in more naturalistic settings. It is reasonable to expect that the *degree* to which psychiatrists and therapists adhere to the guidelines, influences outcome as well. Some studies discussed above also addressed this aspect. In the Texas Medical Algorithm Project greater provider adherence to treatment guideline recommendations was associated with greater reductions in depressive symptoms and in overall psychiatric symptoms over time. Unfortunately, in the Berlin Algorithm Project this aspect was not studied. STAR*D, on the other hand, paid much attention to physicians' adherence to the protocol. Adherence to protocol-specific treatment was monitored based on

presence of symptoms, side effects, and dose and duration of antidepressant drug treatment at each critical decision point during the acute phase treatment of major depression. Feedback was provided by clinical coordinators, assisted by Web-based reports following each treatment visit. In 85% of the patients the first treatment step (with the antidepressant citalopram) was carried out according to the guidelines. Most deviations from treatment recommendations occurred late in treatment and were often justifiable [34]. However, it remains unclear to what extent the enhanced outcomes in trial settings are a result of diligent measurement-based care or of the specific treatment steps that are used. Valid predictors of response are needed to further tailor specific algorithms to individual patients.

Also, when discussing adherence in trials, it is important to emphasize that the generalizability of the results from the building blocks of guidelines, the randomized controlled trials (RCTs) as method to assess efficacy, to the effectiveness of daily practice might be limited by the design of RCTs. Much more than in clinical practice only a selected group of patients are eligible for RCTs and adherence is monitored intensively. The STAR*D trial approached daily practice as much as possible, but still has some properties of an RCT.

Adherence to guidelines in clinical practice

During the last ten years several studies assessing the adherence to guidelines in the clinical practice of mental health have been published. Most studies focused on the adherence to guidelines for one specific disorder, like depressive disorder, bipolar disorder or schizophrenia. The majority of studies assessed only one specific treatment modality, predominantly pharmacotherapy, in frequency followed by pharmacotherapy in combination with psychotherapeutic interventions [35-54]. With respect to indicators for guideline adherence, studies assessed one or more of the following aspects of treatment: choice, dosage or duration of medication, frequency of visits, treatment of co-morbidity and several principles of psychotherapy, the application of case-management and/or treatment-outcomes. The number of indicators used per study varied from only one [37] to 49 [43]. Studies also differed in the way adherence was quantified: some studies differentiated between a low, moderate and high level of adherence [43,45,47] others used percentages. [37,38,55]. Finally, many studies used administrative data to assess adherence, for instance from insurance companies [36,37,41,52,56].

This overview shows that a generally accepted and standardized way to assess guideline adherence has not been developed yet. Importantly, most studies noticed a substantial discrepancy between guideline recommendations and treatment in clinical practice.

Adherence to guidelines in The Netherlands

Since the late 1980's the Dutch government has stimulated implementation of guidelines in order to improve the quality of care, create more cohesion and transparency, and reduce costs [27]. In this respect, it was also stimulated to adapt guidelines to local settings in so-called, programs of care (zorgprogramma's).

In the Netherlands, guidelines are considered important instruments to improve care and in 2004, the Dutch 'umbrella' organization for mental health care, GGZ-Nederland, reported that guidelines were implemented in the majority of the local mental health institute. Surprisingly, however, published data on the actual implementation of guidelines and adherence to guidelines in mental health are still very limited. The lack of (inter) nationally accepted methods of assessing guideline adherence in psychiatric care may play a role here.

Factors influencing adherence in clinical psychiatric practice

Beyond the assessment of the *degree* of guideline adherence lies of course the question what factors influence this. It will not come as a great surprise that, given the absence of a mature methodology to assess adherence in routine psychiatric care, the study of factors influencing adherence is still in its infancy too. Also, as there are many factors that potentially can influence adherence in routine psychiatric care, it is usually not feasible to study all these factors in concert. Most studies, including the ones in this thesis, therefore focus on specific factors. Here we will discuss some of the limited data available for routine psychiatric care, especially with regard to therapist and patient factors. Because of the small number of studies available for routine psychiatric care, we will also discuss results from some studies from other branches of medicine. Obviously, we should not forget that specific characteristics of the guidelines can affect their actual use as illustrated by a meta-analysis that found that

guidelines that are easy to understand or do not require specific resources, have a greater chance to become part of routine care [57].

Clearly, therapist factors do play a role in adherence to guidelines as therapist should prescribe and provide the actual treatments and sequence as described in the guidelines.

A meta-analysis in the United States found that less than 50% of the physicians, including primary care physicians, were aware of the existence of specific guidelines for their specialization. Only ten percent of the physicians that were aware of the existence of guidelines were familiar with the content of the specific guidelines. In addition it was shown that caregivers who are aware of the guidelines do not always follow them. Several barriers to guideline adherence were identified apart from lack of awareness and familiarity: lack of agreement with the content of the guidelines or with working according to guidelines in general, lack of self-efficacy, lack of outcome expectancy, lack of motivation to change previous practice and external barriers (for example time limits or the lack of a reminder system) [58]. Other factors found to affect guideline-adherence in physicians were age and/or experience: young professionals or less experienced ones would be more inclined to use guidelines than older, experienced professionals [57]. In the mental health field, a study assessing adherence to guidelines for the treatment of major depression found that fewer than two-thirds of the clinicians recalled receiving the guidelines, and only half of those who did receive the guidelines, reported having read them [59]. This suggests that it may be useful to invest in the therapists' awareness of guidelines. In the Texas Algorithm Study, therapist education, but also strict trial conditions plus a collaborative approach to medication choice were indeed associated with high levels of adherence [32,33]. Type of profession may be another relevant therapist factor, as shown in a Dutch study using vignettes to investigate the variation in intention-to-treat decisions among four professions involved in the management of depression: 150 general practitioners, 100 psychiatrists, 123 psychotherapists, and 100 clinical psychologists. Almost one third of the decisions was inappropriate. There was considerable variation between the professions: psychiatrists made more appropriate choices than the other professions, but they had also the highest rate of overtreatment [60]. Data from pharmacy and insurance use also showed that patients initially seeing psychiatrists are most likely to receive adequate treatment [61].

The intuitive counterpart of therapist characteristics, patient characteristics, has been shown to affect guideline adherence in different settings. In primary care settings for instance, it has been demonstrated that as many as half of all patients do not adhere closely to their assigned treatment, resulting in negative effects on outcomes and quality of life, and extra costs [62]. In a transplant setting, Adherence among liver transplant candidates was found to be positively correlated with specific personality traits (e.g. agreeableness) and coping strategies (e.g. planning)[63].

In mental health settings, several studies retrospectively analyzed patient characteristics possibly associated with receiving guideline concordant care, but studies assessing patient factors associated with low guideline concordant care across common psychiatric disorders and treatment modalities in routine clinical care are scarce. So far, only a small number of studies has looked at MAS disorders, such as a Dutch study conducted by Prins et al. [64]. This study found that educational level, accessibility of care and patients' perceived needs for care, were positively associated with the delivery of guideline-concordant care for anxiety or depression. Adherence to web-based CBT in adolescents applying for an online depression and anxiety intervention program was predicted by the scores on a questionnaire, the Goldberg Depression and Anxiety scales [65]. Severity of symptomatology, but also low motivation, was also found to affect compliance in another study of depressed patients treated with CBT. Severity and motivation probably interfered with doing homework and attending follow-up appointments [65].

Several other studies in the mental health field focused on outpatients with non-MAS psychiatric disorders [65-73]. In these studies younger age, male gender, lower socioeconomic status, minority status and poorer social functioning were all found to be associated with adherence problems. Additional factors associated with low adherence were poor insight, having a co-morbid psychiatric disorder and (severe) side effects of psychotropic medication.

In conclusion, the available data suggest that patient and therapist factors do influence adherence to guidelines for MAS disorders in routine clinical practice, and hence, taking these factors into account might be relevant for decision-making or optimization of care, but further research is warranted. Clearly, this research field would also benefit from standardized and easy applicable approaches for assessment of adherence in clinical practice.

Leiden Routine Outcome Monitoring project

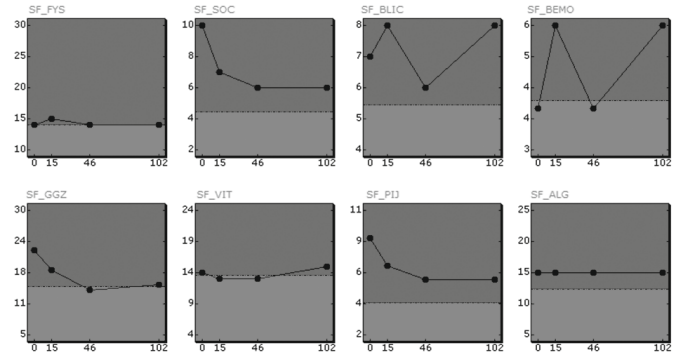
The studies described in this thesis were performed at Rijnveste, a psychiatric outpatient clinic in Leiden and part of the Regional Mental Health Provider Rivierduinen.
Rijnveste is part of Rivierduinen, a regional mental health care provider in the Netherlands providing secondary mental health care for an area with over one million inhabitants. The use of evidence based guidelines and Routine Outcome Measurement (ROM) is integrated in routine practice in Rivierduinen. The implementation of guidelines and a system for ROM started in 2002, in collaboration with the Department of Psychiatry of the Leiden University Medical Hospital. The local stepped care-based programs followed the national multidisciplinary guidelines and were slightly adjusted to the local setting (most importantly by adding ROM as an element of treatment). For some studies in the thesis data from the Leiden ROM project are used. For a detailed description of ROM see box 1.1.

Box 1.2. ROM in the Leiden University Medical Centre and Rivierduinen

In spring 2002, the Regional Mental Healthcare Provider (RMHP) Rivierduinen (an institute serving a region with more than 1 million inhabitants) and the Department of Psychiatry of the Leiden University Medical Centre (LUMC) started collaboration for routine assessment of Diagnostic Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) diagnoses as well as symptom severity, wellbeing, and generic health status at intake and follow-up. This project is known as Routine Outcome Monitoring (ROM).
Initially, ROM was restricted to patients who were referred for treatment of mood, anxiety, and/or somatoform (MAS) disorders. These patients form a relatively homogenous group with substantial mutual comorbidity [74] who mainly receive outpatient care. To be eligible, patients must have sufficient mastery of the Dutch language, and have to be able to complete self-report questionnaires. Patients who are considered (by their clinician) to be too ill to complete questionnaires or refuse assessment are excluded from ROM.
Patients are assessed by psychiatric research nurses who have been extensively trained and supervised. Assessments are scheduled at intake, at three- to four-month intervals during follow-up, at the start of a new

treatment step, and at the end of treatment. During the first session, a standardized diagnostic interview (the Mini-International Neuropsychiatric Interview-plus, MINI-plus) [75] is administered to determine DSM-IV-TR axis-I diagnoses. In addition, socio-demographic characteristics are assessed and maladaptive personality traits are identified with the Dimensional Assessment of Personality Pathology Short Form (DAPP-SF) [76]. At baseline and at follow-up, a number of self-report as well as observer-rated generic and disorders specific symptom severity scales are administered in order to monitor change in symptom reduction, wellbeing, and general functioning [77]. All instruments are commonly used in treatment-outcome research and have good psychometric properties as demonstrated by national and international publications. An overview of instruments used is available at lumc.nl/psychiatry/rom-instruments. To date, treatment information has not been documented in ROM.

Results are summarized in a report which is discussed with the patient by the clinician and which is used to evaluate treatment. In addition, data are anonymized and used for scientific research. As data collection is integrated in standard care and data are anonymized, patients are not required to provide informed consent. The use of the anonymized data for scientific purposes has been approved by the Medical Ethical Committee of the LUMC



Source: Based on thesis Van Noorden, 2012, On real-world patients and real-world outcomes: The Leiden Routine Outcome Monitoring Study in patients with mood, anxiety and somatoform disorders; p22. With permission from the author.

Aim of the studies and outline of the thesis

The overall aim of this thesis is to develop a set of reliable, valid and easy applicable factors that can be used to assess guideline adherence across multiple MAS disorders and treatment modalities in routine clinical practice.

In chapter 2 we describe a study on the extent of poor treatment response in a typical Dutch routine psychiatric outpatient setting for MAS disorders, the outpatient clinic of Rijnveste, part of the Regional Mental Health Provider Rivierduinen. If the frequency of a good treatment response is very high already, there is of course no need to try to improve response by assessing and ameliorating guideline adherence.
In chapter 3 we embark on research into implementation and adherence in routine psychiatric care by conducting a survey among the boards of the Dutch mental health institutes on the perceived rate of implementation and adherence in their institutes.
In chapter 4 we develop and validate a set of disorder independent process indicators based on the guidelines for treatment of specific common mental disorders (i.e. mood, anxiety or somatoform disorders). With this set of indicators we retrospectively examine the overall level of adherence to clinical guidelines in three consecutive years in a randomly selected sample of 300 MAS outpatients from Rijnveste who started an acute phase psychiatric treatment. Patients were treated with pharmacotherapy, psychotherapy or a combination of both.
In chapter 5 and 6, we examine patient and modality/therapist factors potentially influencing adherence in routine psychiatric outpatient practice. First, in chapter 5, we examine whether treatment modality is a factors that significantly influences guideline-adherence.
In chapter 6, we subsequently examine what socio-demographic and psychometric characteristics of patients available in ROM data are associated with guideline adherence as assessed with our indicators. In chapter 7, we examine in a proof-of-principle whether not only ROM data, but also routinely collected administrative data of outpatients treated for MAS in Rivierduinen, can be used to assess adherence with our set of disorder independent process indicators.

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