Economic Evaluation of Psychotherapy for Personality Disorders:

burden of disease, cost-effectiveness, and the value of further research and active implementation

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Economische Evaluatie van Psychotherapie voor Persoonlijkheidsstoornissen:

ziektelast, kosteneffectiviteit en de waarde van verder onderzoek en actieve implementatie

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General introduction

Personality disorders are among the most common mental disorders in the general population[1,2] and mental healthcare settings[3,4] with reported prevalence rates of 13.4 and 45.5 percent, respectively. Personality traits are pervasive and enduring patterns of the ways individuals perceive, relate to, think about, and behave within their environment. When these traits become inflexible and maladaptive they constitute personality disorders. The general diagnostic criteria for personality disorders according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth edition, Text Revision (DSM-IV-TR) of the American Psychiatric Association[5] are presented in **Table 1.1**. Personality disorders can be categorized into three clusters. Cluster A contains the odd or eccentric disorders, including paranoid, schizoid, and schizotypal personality disorder; cluster B covers the dramatic, emotional or erratic disorders, including borderline, antisocial, histrionic, and narcissistic personality disorder; and cluster C consists of the anxious or fearful disorders, including avoidant, dependent, and obsessive-compulsive personality disorder.

Table 1.1 General diagnostic criteria for a DSM-IV-TR Axis II personality disorder (APA, 2000)

According to DSM-IV-TR, the diagnosis of a personality disorder must satisfy the following general criteria, in addition to the specific criteria listed under the specific personality disorder under consideration.

A. An enduring pattern of inner experience and behavior deviating markedly from the expectations of the individual's culture. This pattern is manifested in two (or more) of the following areas:
   (1) cognition (perception and interpretation of self, others and events)
   (2) affect (the range, intensity, lability and appropriateness of emotional response)
   (3) interpersonal functioning
   (4) impulse control

B. The enduring pattern is inflexible and pervasive across a broad range of personal and social situations.

C. The enduring pattern leads to clinically significant distress or impairment in social, occupational or other important areas of functioning.

D. The pattern is stable and of long duration and its onset can be traced back at least to adolescence or early adulthood.

E. The enduring pattern is not better accounted for as a manifestation or consequence of another mental disorder.

F. The enduring pattern is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., head trauma).

A sense of urgency

In January 2004, the Dutch government intended to cut down the federal budget by restricting the number of psychotherapy sessions that were reimbursed in treating personality disorders. The psychotherapeutic community was enraged by this new development and grouped together to try to reverse the measure. Partly due to this intense reaction the government started an investigation about the potential savings of its own imposed measure, which surprisingly indicated that restricting the number of psychotherapy sessions for personality disorders would lead to even higher costs in other areas of health care.[6] Although the measure was relaxed in January

2007, this sequence of events contributed significantly to the awareness within the psychotherapeutic community that evidence was needed that could justify the often expensive treatment strategies for patients with personality disorders.

Currently available evidence

A multidisciplinary clinical guideline in The Netherlands recently identified various modalities of psychotherapy to be preferential for personality disorders based on strong evidence of efficacy.[7] However, these recommendations were informed by limited evidence about the economic impact or cost-effectiveness of the treatment strategies. This evidence gap was previously reported by a 2007 review in which our research group evaluated the existing evidence about the effectiveness, cost-effectiveness, and necessity of psychotherapy in treating personality disorders.[8] The review highlighted that while effective treatments are available, the evidence on cost-effectiveness of treatment strategies, which is needed to inform policy debates regarding psychotherapy, was lacking. A promising initiative of the Dutch Foundation of Clinical Psychotherapy indeed monitored cost and effects among inpatients in mental health care institutes offering specialized psychotherapy. Although this study indicated a high burden of disease,[9] the omission of standardized diagnoses and the limited assessment battery prevent us from using these data to draw conclusions about personality disorders per se or conducting a state of the art economic evaluation.

Economic evaluation

Cost-effectiveness analyses are increasingly being used to inform policy decisions regarding the adoption and reimbursement of health interventions. When the objective of the health care system is to maximize health gains subject to a budget constraint, a standard approach to identifying an optimal set of interventions is through cost-effectiveness analysis. When current practice is more effective and costs the same compared to a new alternative or current practice has the same effectiveness but is less expensive than the alternative, then current practice is undoubtedly the preferred option. However, the decision gets complicated when the proposed alternative is more effective but also more costly than current practice or less effective but also less costly; in such circumstances the decision must be made as to whether the additional health benefits of the more effective treatment are worth the additional cost.[10] This information can be represented by the incremental cost-effectiveness ratio (ICER), i.e., the additional cost divided by the additional health benefit between one strategy and the next-less-costly treatment strategy. The ICER is often expressed as costs per quality-adjusted life year (QALY) gained. If the ICER of a health intervention is less than the decision maker's willingness-to-pay (WTP) for an additional unit of health gain, then the health intervention is considered to be cost-effective. The "most cost-effective" strategy is the strategy with the highest ICER below the WTP threshold, representing the option that yields the highest level of benefit for its cost.

The societal perspective is often recommended as the preferred viewpoint in an economic evaluation. That is, all relevant costs irrespective of payer are included, which allows one to capture costs that are incurred in one area of health care that may well lead to savings elsewhere.

SCEPTRE trial

The Study on the Cost-Effectiveness of Personality disorder TREatment (SCEPTRE) was conducted with the purpose of providing data for the economic evaluation of various psychotherapeutic treatments for personality disorders. The 1,708 patients who entered this study were recruited from March 2003 to March 2006 from six mental health care institutes in The Netherlands offering specialized psychotherapy for adult patients with a diagnosis of DSM-IV personality disorders. Exclusion criteria were psychotic disorders (e.g., schizophrenia), organic cerebral impairment, and mental retardation. Comorbid Axis I and Axis II disorders were allowed. Patients completed an extensive assessment battery including a semi-structured interview for diagnosing personality disorders, and a generic quality of life measure. The cost calculations included direct medical costs (i.e., primary treatment costs and costs of health care utilization) and direct non-medical costs (i.e., lost productivity due to time spent in treatment), as well as indirect costs (i.e., past and future lost productivity due to disease). The 922 patients who were assigned to treatment, based on the assessment battery combined with the expert opinion of clinicians, were included in the study and followed for three years. To overcome the problem of selection bias in the naturalistic design of the study, we controlled for initial differences in patient characteristics with the propensity score method.

The treatments in the six institutes differ widely in terms of setting, duration, intensity, theoretical framework, and therapeutic techniques. This study compares dosage, specified by a combination of treatment setting (outpatient, day hospital, and inpatient) and duration (short-term or up to six months versus long-term or more than six months). In the short-term outpatient strategy, patients are offered up to two sessions per week of individual or group psychotherapy for up to six months. In the long-term outpatient strategy, patients are offered the same for more than six months. In the short-term day hospital strategy, patients are offered psychotherapy combined with sociotherapy and/or non-verbal therapies for one to five days per week for up to six months. In the long-term day hospital strategy, patients are offered the same for more than six months. The inpatient strategy also offers psychotherapy combined with sociotherapy and/or non-verbal therapies, but patients reside in the treatment centers five days per week. The therapists were licensed psychiatrists or psychologists.

Objective of the thesis

This dissertation provides insights into three questions that need to be addressed by any health care system in order to optimize allocation of health care resources: (1) Based on currently available evidence, how cost-effective is it to reimburse a health intervention?, (2) Is it cost-effective to fund research to collect further evidence to inform the reimbursement decision in the future?, and (3) Is it cost-effective to invest in active implementation of the cost-effective health interventions? The aim of the first two dissertation chapters was to investigate the burden of disease among treatment-seeking personality disorder patients in terms of quality of life (Chapter 2) and societal costs (Chapter 3). These findings can serve as a guide in setting the cost-effectiveness threshold which is necessary to inform reimbursement decisions. In Chapter 4 and Chapter 5 we provide an answer to the first question by exploring whether cost-effective treatment strategies are available in treating cluster B and C personality disorders. In Chapter 6 the second and third questions are addressed by calculating the societal value of conducting further research to inform reimbursement decisions and implementation of cost-effective treatment strategies for cluster B and C personality disorders. The general discussion, in Chapter 7, summarizes our findings and discusses the implications for clinical practice and recommendations for further research.

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The Burden of Disease in Personality Disorders: Diagnosis-Specific Quality of Life

Chapter 2

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Abstract

A generic quality of life measure was used to investigate the burden of disease in a large sample of patients with personality disorders. The 1,708 subjects included in this study were recruited from six different mental health care institutes in the Netherlands. The burden of disease was measured using the EuroQol EQ-5D. Personality disorders were diagnosed using the Structured Interview for DSM-IV Personality (SIDP-IV). The mean EQ-5D index value was 0.56. Primarily the total number of personality disorder diagnoses rather than the specific type determined the quality of life. Notably borderline personality disorder was not associated with the highest burden. The findings indicate that patients with personality disorders experience a high burden of disease, comparable to that of severe somatic illnesses. The results call into question the primary focus in literature on borderline personality disorder. The current study yields a strong argument in favor of reimbursing (effective) treatments for this patient population.

Introduction

Personality disorders are known to be associated with significant impairment in social, occupational, and other important areas of functioning. Several studies indicate poorer social and interpersonal functioning, and poorer occupational functioning, satisfaction, and achievement among patients with personality disorders as compared with others.[1,2] On measures of global functioning, most studies have shown significant functional impairments for patients with personality disorders.[3,4,5] A study by Skodol and colleagues,[6] for instance, compared the psychosocial functioning in patients with personality disorder (schizotypal, borderline, avoidant, and obsessive-compulsive) with major depressive disorder. They found patients with schizotypal and borderline personality disorder to be more impaired than patients with obsessive-compulsive personality disorder or major depressive disorder. This impairment is remarkable because impairment in major depressive disorder has been found to be comparable to that of chronic medical illnesses such as diabetes and arthritis.[7,8] A study of outpatients by Nakao, Gunderson, and Phillips,[9] showed that patients with any personality disorder are more functionally impaired (GAF-scores) than those without a personality disorder.

All these investigations studied the "functioning" in personality disorder patients. However, in contemporary research, more and more emphasis is put on the "subjective quality of life" of these patients. This paradigm shift is reinforced by a number of studies showing that it is the patients' subjective well being, rather than objective medical condition, that determines their treatment-seeking behavior, their compliance and their evaluation of treatment.[10] Furthermore, quality of life has become an important outcome in cost-effectiveness analysis.[11] As a consequence, the interest of psychologists and psychiatrists is no longer limited to symptom-focused outcome assessment, as they have become aware of the importance of quality of life measures in their clinical outcome measures. In a recent Norwegian study, the quality of life of 72 patients with personality disorders in a psychiatric outpatient clinic was examined.[12] The investigators used the multi-dimensional Short Form 36 (SF-36), a standardized generic measure, to assess the quality of life. The main finding of this study was that personality disorder patients treated in a psychiatric outpatient clinic had a significantly lower quality of life, on both the physical and mental SF-36 dimensions, than an age- and gender-adjusted general population sample. Furthermore, in a group of 1651 inpatients with complex personality problems and personality disorders, Soeteman, Timman, Trijsburg, Verheul, and Busschbach[13] found a severe impairment in quality of life (EuroQol EQ-5D index score of .54). They compared the quality of life in this mental condition with those in severe somatic illnesses such as Parkinson's disease (EQ-5D index score = .58) and rheumatic disease (EQ-5D index score = .53). Both studies described above have to be considered explorative studies of quality of life in personality disorders. The Norwegian study used a small sample of 72 psychiatric outpatients, and has therefore a limited external validity. Soeteman and colleagues' sample size was substantial, but no standardized Axis II diagnoses were available; thus the results have limited internal validity.

The aim of this study is to investigate the relation of the burden of disease in terms of quality of life with the 14 DSM-IV personality disorders using a generic quality of life questionnaire, i.e., the EuroQol EQ-5D. Such a generic instrument can measure the burden of disease regardless of patients' diagnoses and can therefore be used to compare the burden of disease in patients with personality disorders with patients with other medical conditions, for example severe somatic illnesses. Moreover, the different dimensions of quality of life in the EQ-5D are combined into one weighted score, thereby yielding unambiguous comparisons. Note that in

this investigation we assume an inverse relation between quality of life and burden of disease; this assumption is also made in the Global Burden of Disease project of the WHO.[14]

Method

Participants

Participants were recruited from a consecutive series of admissions to six mental health care institutes in the Netherlands offering outpatient, day hospital, and/or inpatient psychotherapy for adult patients with personality pathology and/or personality disorders. As part of the standard admission procedure, all applicants performed a routinely distributed assessment battery including self-report questionnaires in order to measure psychopathology, personality, functional impairments, and treatment history, and a semi-structured interview for diagnosing personality disorders. When the administration of the questionnaires forms part of the routinely administered clinical intake procedure and does not involve additional risks or load, informed consent is not mandatory under Dutch law. For this reason, informed consent was only asked if the patient participated in any further follow-up investigations.

From March 2003 to March 2006, 2,540 individuals have been registered as admissions to the six mental health care institutes. Of these patients, 462 (18.2%) did not start and 272 (10.7%) did not complete the formal admission procedure. Of the remaining 1,806 patients, 46 were excluded due to clear signs of unreliable data in the interview and/or questionnaires (2.3%) or due to serious intellectual impairment (0.3%). The EQ-5D was missing or incomplete for 52 patients, leaving 1,708 patients for the current study sample, i.e., 94.6% of those who completed the formal assessment procedure. Of these patients, 35.4% were male. The mean age was 33.7 years (SD 9.9, range 18–67). Of these, 65.6% were unmarried, 22.0% married, and 12.4% were divorced or widowed. No differences with respect to gender, age, and educational level were found between those admissions that were included as compared to those who were excluded from the sample.

Measures

The quality of life was measured using the EuroQol EQ-5D.[15] The descriptive system of the EQ-5D records quality of life in 5 dimensions: mobility (walking about), self-care (washing and dressing oneself), usual activities (e.g., work, study, housework, family, or leisure activities), pain/discomfort and anxiety/depression. Each dimension is divided into 3 response levels: no problems, some or moderate problems, and extreme problems or unable to. The combination of scores define a total of 243 different possible health states and each of these are weighted to arrive at a single index score between –0.33 (worst imaginable health state) and 1.00 (best imaginable health state). The Dutch norm scores were used for calculating the mean EQ-5D index values.[16]

Personality disorders were measured using the Dutch version of the Structured Interview for DSM-IV Personality[17] (SIDP-IV; translated by De Jong et al.[18]). This instrument includes the 11 formal DSM-IV-TR Axis II diagnoses (e.g., schizoid personality disorder) including personality disorder mixed, the two DSM-IV-TR appendix diagnoses (depressive and negativistic personality disorder), and—in addition—the DSM-III-R self-defeating personality disorder. Interviewers were master-level psychologists, who were trained thoroughly by one of the authors (RV), and who received monthly booster sessions to avoid drift from the interviewer guidelines.

Inter-rater reliability was computed in 30 videotaped interviews rated by three observer raters. Percentage agreement ranged from 84% (avoidant PD) to 100% (schizoid; median 95%). Intraclass correlation coefficients (ICC) for the sum of DSM-IV personality disorder traits present (i.e., scores "2" or "3") ranged from 0.60 (schizotypal) through 0.92 (antisocial; median 0.74).

Statistical analysis

A multiple regression main effect analysis was conducted, measuring the independent contribution of the different diagnoses on quality of life. The majority of patients (54.9%) received at least two personality disorder diagnoses. That is the reason an additional regression was performed to account for possible interactions between diagnoses. Because the number of possible interactions between 14 independent variables becomes intractable, the interaction term is represented by a count of the diagnoses given. Age, gender, and education (socioeconomic status) variables are associated with quality of life and were therefore entered into the multiple regression models.[15]

Results

In **Table 2.1**, the rank ordering of the quality of life figures is displayed for the 14 specific DSM-IV personality disorders. Because patients can have more than one personality disorder, the sum of the number of patients in the different diagnostic groups is higher than the total number of patients included in this study.

The mean EQ-5D index value for the personality disordered group as a whole was .56 (SD = .27), representing a severe burden of disease. Note that the mean EQ-5D index scores for almost all of the specific diagnostic groups (except for PD mixed and schizotypal personality disorder) in **Table 2.1** appear to be lower than the mean EQ-5D index score for the total group of patients with at least one disorder (.56). This is possible because patients with a large number of diagnoses, and concordantly a low quality of life (see also **Table 2.2**), are represented in an equally large number of diagnostic groups. As a consequence of their poor quality of life, they "lower" the mean EQ-5D index scores of all of these groups.

In the present sample, depressive (32.0%), avoidant (28.5%), obsessive-compulsive (20.8%), and borderline personality disorder (20.8%) were the most frequently diagnosed disorders. Schizotypal (0.9%) and schizoid personality disorder (1.1%) were the least frequently diagnosed disorders. In about one-fifth of the total group of patients no personality disorder could be diagnosed.

When studying the main effects of the specific personality disorders in a linear regression analysis, six out of 14 appeared significant ($p < 0.05$), indicating that having or not having that specific disorder has a significant effect on the quality of life in this sample. These six disorders are borderline, narcissistic, obsessive-compulsive, depressive, negativistic personality disorder, and personality disorder mixed.

Table 2.1 EuroQol EQ-5D index scores (mean and standard deviation) for the 14 DSM-IV personality disorders

					Analysis	
Personality disorder	**N**	**%**	**EQ-5D**	**SD**	**ß [1]**	**p**
Personality disorder mixed	255	14.9	.62	.27	-0.05	0.05
Schizotypal	15	0.9	.56	.30	0.02	0.49
Avoidant	487	28.5	.54	.26	-0.04	0.16
Obsessive-compulsive	356	20.8	.53	.27	-0.06	0.02
Borderline	356	20.8	.52	.28	-0.07	0.01
Antisocial	36	2.1	.52	.30	-0.03	0.26
Dependent	179	10.5	.52	.27	-0.03	0.22
Paranoid	102	6.0	.51	.28	0.00	0.92
Narcissistic	99	5.8	.51	.30	-0.08	0.00
Schizoid	18	1.1	.51	.28	-0.03	0.21
Depressive	546	32.0	.50	.27	-0.17	0.00
Histrionic	49	2.9	.50	.26	-0.01	0.83
Self-defeating	116	6.8	.48	.28	-0.03	0.22
Negativistic	61	3.6	.42	.28	-0.06	0.01
N with at least one personality disorder	1396	81.7	.56	.27		
N without personality disorder	312	18.3	.67	.25		

[1] Linear regression analysis: dependent variable quality of life; independent variables categorical diagnoses: having or not having that particular personality disorder

Table 2.2 EuroQol EQ-5D index scores (mean and standard deviation) for increasing number of personality disorder diagnoses

Number of PDs	**N**	**%**	**EQ-5D index score**	**SD**
No PD	312	18.3	.67	.25
One PD	458	26.8	.62	.27
Two PDs	365	21.4	.58	.26
Three PDs	279	16.3	.55	.27
Four PDs	168	9.8	.48	.28
Five PDs	76	4.4	.50	.26
Six PDs	26	1.5	.42	.28
Seven or more	24	1.4	.32	.23

Table 2.2 shows that the quality of life is inversely associated with the number of personality disorders diagnosed. As could be predicted from the lower means for specific diagnoses compared to the overall mean in **Table 2.1**, the number of personality disorders has a large effect

on quality of life (p = 0.000). When controlling for the number of disorders in the regression analysis, only depressive personality disorder maintains a unique statistically significant effect on quality of life (p = 0.03).

Discussion

Personality disorders are associated with a severe impairment in quality of life. The overall EQ-5D index value of .56 suggests that the quality of life experienced by patients with personality disorders can be compared to the quality of life in, for instance, rheumatic disease, lung cancer, or Parkinson's disease with EQ-5D index scores of .53, .58, and .58, respectively.[19,20,21] The burden of having a personality disorder seems even higher than in patients with type II diabetes (EQ-5D score of .69),[22] schizophrenia outpatients treated with neuroleptics (.73),[23] and HIV infected patients (.77).[24] The burden is only found to be higher in major depressive disorder (.33)[25] and patients with renal failure on heamodialysis (.44).[26] It can be concluded that patients who are in search for treatment for their personality disorders experience a high burden of disease, as compared to other populations with severe somatic illnesses.

Borderline, narcissistic, obsessive-compulsive, depressive, negativistic personality disorder and personality disorder mixed appear to have a significant effect on the quality of life. However, when the total number of personality disorders diagnosed is taken into account and included in the analysis, the latter appears the most important predictor of quality of life, leaving only the depressive personality disorder with an additional effect. These findings seem to imply that in patients with borderline, narcissistic, obsessive-compulsive, negativistic personality disorder, and personality disorder mixed the comorbidity of other Axis II disorders rather than the specific diagnosis caused the quality of life to be more impaired. This conclusion is in line with the results of a study by Jackson and Burgess,[27] in which no significant differences could be found on the SF-12 Mental Summary Scale between eight ICD-10 personality disorders in an Australian community sample of 10,641 participants. Consistently, the authors mentioned that the addition of other comorbid personality disorders to the specific personality disorders led to sizeable increases in the odds ratios for all personality disorder types on the disability measures. Similar results were found by Nakao et al.,[9] who showed a strong positive relationship between the total number of Axis II criteria met and the severity of the functional impairment as measured with the Global Assessment of Functioning Scale (GAF score). Jackson and Burgess[28] also found an increasing disability according to the SF-12 Mental Summary Subscale with an increasing number of personality disorders. The only exception seems the study by Narud et al.[12] who found no worsening of quality of life as measured with the SF-36, with increasing number of personality disorders. They attributed this to a small sample size.

The 1,708 participants included in this study were recruited from six different mental health care institutes in the Netherlands specialized in the psychotherapeutic treatment of personality problems and disorders. The large number of patients and the different settings can be considered one of the strengths of this study, as these enhance the external validity of the results. On the other hand, we only sampled patients that were referred to some sort of psychotherapy; therefore the results may not be generalized to all prevalent cases in the community. However, this cannot be considered legitimate criticism taken into account the aim of the study. The ultimate purpose of our study is providing an argument for reimbursing, in other words providing an answer to the question if an expensive treatment for this population of patients, based on the

necessity of treatment (i.e., burden of disease), is justified. Only personality disordered patients who actually search for, or are referred to, some sort of treatment will claim money for that treatment, which is paid for by society.

Another limitation of our study is that no standardized diagnoses of comorbid Axis I psychiatric disorders were available. Note, however, that this limitation does not jeopardize the main finding of our study, namely that patients who seek treatment for their personality disorders experience a high burden of disease. In this stage of their disorder, when patients are admitted to a mental health care facility, it is difficult to find patients with "only" Axis II problems. Isolating the effects of the Axis I disorders would be the same as considering the burden of disease of diabetics without the foot ulcers or the quality of life of schizophrenic patients without the symptoms caused by neglect. Moreover, it has been shown that Axis I and Axis II disorders are independently related to disease-specific burden of disease parameters.[28,29,6,30] The independent contribution of Axis I and Axis II pathology to the burden of disease should be addressed in future research.

The use of generic quality of life measures in mental health research has been criticized.[31] According to Chisholm and colleagues, one of the concerns is that the domains of particular importance in the measurement of quality of life in people with mental health problems are not represented properly in the prominent generic quality of life measures employing domains of physical mobility, pain, and disability. They argue that this can lead to an undervaluation of the burden of disease in the mentally ill. Another concern is that mental disorders are perceived as more heterogeneous in the course, content, and consequences over time than somatic disorders, which causes the quality of life in mental disorders to have a limited predictability and stability.

However, this study provides evidence that these concerns are not justified for the patient population subject to our investigation. A substantial burden of disease was found by using the generic EuroQol EQ-5D, which at least indicates that an important part of the problems in this particular patient group are well captured in the 5 domains of the EQ-5D. Moreover, a similar high burden of disease (EuroQol EQ-5D index score of .54) was found in an earlier study of Soeteman et al.[13] among a large group of patients with similar problems, which indicates the robustness of the present findings. Additionally, the reliability and validity of quality of life measures have been established in other mental illnesses, such as schizophrenia.[32] The present demonstration of the use of the EQ-5D in personality disorders should encourage its use in research, which should help positive funding decisions since it is easier to make comparative decisions across disease types using generic quality of life measures such as the EQ-5D.

When examining the ranking of the burden of disease in the 14 specific DSM-IV personality disorders in **Table 2.1**, it becomes clear that a high burden is not necessarily associated with receiving more attention in clinical research. Blashfield and Intoccia[33] have shown that the only personality disorder whose literature was clearly alive and growing was that of the borderline personality disorder; a disorder that is positioned in the upper regions of the ranking of quality of life. On the other hand personality disorders that are associated with a higher burden, according to our ranking, have either very small literatures (e.g., dependent, narcissistic, paranoid, passive-aggressive) or literatures with flat or negative growth rates (e.g., dependent, histrionic, paranoid, passive-aggressive, schizoid). One explanation is that the disorders that cause the greatest societal burden (e.g., antisocial) or the greatest burden to clinicians (e.g., borderline) have traditionally attracted most scientific attention. Our findings suggest that an emphasis on

burden from the patient perspective would have lead to completely different choices.

In health care, cost-effectiveness analyses are a well-established decision tool in reimbursement policy. However, a growing body of evidence suggests that cost-effectiveness alone is not sufficient for rational decision making in this regard. It is found that burden of disease interacts with cost-effectiveness considerations: the higher the burden of disease, the more willing society is to accept a poor cost-effectiveness.[34,35] For instance, the cost-effectiveness of Viagra is very favorable, but its funding remains in dispute. On the other hand, lung-transplantation is known for its unfavorable cost-effectiveness, yet the reimbursement is not a matter of debate. It thus seems that the burden of the patients (or how pitiful their situation seems) also plays a key role in the discussion which treatments to fund. More and more existing treatments, which have long been reimbursed without providing any evidence for their cost-effectiveness such as, for instance, psychotherapy, are recently required to demonstrate their efficiency in order to free budget for the treatments, which have already shown to be cost-effective. The current study, showing a high burden of disease in patients with personality disorders, yields a strong argument in favor of reimbursing (effective) treatments for this patient population.

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The Economic Burden of Personality Disorders in Mental Health Care

Chapter 3

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Abstract

Objective

Some evidence suggests that personality disorders are associated with a high economic burden due to, for example, a high demand on psychiatric, health, and social care services. However, state-of-the-art cost studies for the broad range of personality disorder diagnoses are lacking. The current study examines the direct medical costs, as well as the indirect costs, of patients seeking mental health treatment with DSM-IV personality disorders.

Method

The 1740 subjects included in this study were recruited from March 2003 to March 2006 from 6 different mental health care institutes in the Netherlands specializing in the psychotherapeutic treatment of personality disorders. The direct and indirect costs were assessed using the Trimbos and Institute for Medical Technology Assessment Questionnaire on Costs Associated with Psychiatric Illness. Personality disorders were diagnosed using the Structured Interview for DSM-IV Personality.

Results

The mean total costs of the personality disorder group in the 12 months prior to treatment were €11,126 per patient. Two thirds (66.5%) of these costs consisted of direct medical costs, while the remaining costs were related to productivity losses. Borderline and obsessive-compulsive personality disorders were uniquely associated with increased mean total costs.

Conclusion

Treatment-seeking patients with personality disorders pose a high economic burden on society, a burden substantially higher than that found in, for instance, depression or generalized anxiety disorder. These high societal costs present a strong argument in favor of prioritizing effective personality disorder treatments in reimbursement decisions.

Introduction

Hardly any research exists on the economic burden of personality disorders. This is remarkable as the presumed high societal costs of personality disorders are often used as an argument to justify the costs of expensive treatments (in general) for this patient group. Moreover, the economic burden of other mental conditions has already been extensively investigated, for example schizophrenia[1-3] and depression.[4-6]

The limited evidence available so far suggests that personality disorder patients are extensive users of psychiatric services and other mental health care resources.[7,8] Furthermore, there is evidence of a high demand on health, criminal, and social care services.[9-11] The study by Bender and colleagues[7] on the utilization of mental health treatment in 664 treatment-seeking patients found that patients with personality disorder (schizotypal, borderline, avoidant, and obsessive-compulsive) showed more extensive histories of psychiatric outpatient, inpatient, and psychopharmacologic treatment than the comparison group with major depressive disorder without personality disorder. Another study on the service usage of 24 patients with personality disorders calculated that the costs of psychiatric and prison services 1 year prior to treatment were £13,966 per patient.[9]

Other research suggests that – in addition to these health, criminal, and social care service costs – a strong relationship exists between reduced productivity (absence from and inefficiency at work) and mental disorders, including personality disorders.[12-14] For instance, Lim and colleagues[12] studied lost productivity among full-time workers with mental disorders in a community sample of 4579 respondents. Although they found only depression to be significantly associated with more work loss days (number of days unable to perform usual activities), they also found that depression, generalized anxiety disorder, and personality disorder were significantly associated with more "cutback days" (i.e., the number of days on which usual activities were restricted). When the prevalence of these DSM-IV disorders in the Australian community was taken into account, the economic burden of personality disorders dominated over the burden of diagnoses of mood, anxiety, and substance use disorders.

A state-of-the-art economic assessment always includes 2 different types of costs: (1) direct costs related to actual expenditures for detecting and treating the medical problems, and (2) indirect costs associated with lost productivity related to health problems.[15] None of the studies presented so far have combined these 2 aspects, so actually they are incomplete cost-of-illness studies. The only study that did include both direct and indirect costs was a study by Rendu and colleagues.[16] In a follow-up of 303 general practice attendees, this study found that people with personality disorders were nearly twice as costly to support (mean = £3,094 per annum) as those without (mean = £1,633 per annum). This study did not, however, distinguish between the various types of personality disorders.

In sum, the full economic burden of personality disorders has received little attention as compared to other mental illnesses. Moreover, state-of-the-art cost investigations for the broad range of specific DSM-IV personality disorders are lacking. The aim of the present cost-of-illness study was to calculate the direct (use of medical resources) and indirect (productivity losses because of absence from work and reduced efficiency at work) costs of treatment-seeking patients with different diagnoses of personality disorders in order to assess their economic burden on society. This economic burden may not be interpreted as the reduction in costs as a consequence of a new effective intervention, as the costs of the intervention are unknown. However, a cost-

of-illness study may serve as a tool in designing a cost-effectiveness study, as it provides valuable information on which cost items should be included.

Method

Participants

Subjects were recruited from a consecutive series of admissions to 6 mental health care institutes in the Netherlands offering outpatient, day hospital, and/or inpatient psychotherapy for adult patients with personality pathology and/or personality disorders. As part of the standard admission procedure, all applicants performed a routinely distributed assessment battery including self-report questionnaires in order to measure psychopathology, personality, functional impairments, and treatment history and a semistructured interview for diagnosing personality disorders. When the administration of the questionnaires forms part of the routinely administered clinical intake procedure and does not involve additional risks or load, informed consent is not mandatory under Dutch law. For this reason, informed consent was only asked if the patient participated in any further follow-up investigations. The current study design was approved by the Dutch medical ethics committee.

From March 2003 to March 2006, 2540 individuals were registered as admissions to the 6 mental health care institutes. Of these patients, 462 (18.2%) did not start and 272 (10.7%) did not complete the formal admission procedure. Of the remaining 1806 patients, 46 were excluded due to clear signs of unreliable data in the interview and/or questionnaires (2.3%) or due to serious intellectual impairment (0.3%). The questionnaire for estimating costs was missing for 20 patients, leaving 1740 patients for the current study sample, i.e., 96.3% of those who completed the formal assessment procedure.

Of these patients, 35.2% were male. The mean age was 33.9 years (SD = 9.9; range, 18-67 years). Regarding the marital status, 65.2% were unmarried, 22.1% were married, and 12.7% were divorced or widowed. No differences with respect to gender, age, and educational level were found between those admissions that were included as compared to those who were excluded from the sample.

Instruments

The Trimbos and Institute for Medical Technology Assessment (iMTA) Questionnaire on Costs Associated with Psychiatric Illness (TiC-P) was used to collect data on direct and indirect costs.[17] The first part of the TiC-P consists of questions on (1) the number of visits to a general practitioner, psychiatrist, medical specialist (that is, medical professional working at a hospital), physiotherapist, and alternative health practitioner; (2) the day care/ hospital lengths of stay; and (3) the use of medication in the 4 weeks prior to filling out the questionnaire. Bottom-up methodology was used to calculate the total direct medical costs; that is, the total number of medical visits (outpatient visits, hospital lengths of stay, use of medication, etc.) was multiplied by the 2003 unit prices of the corresponding health care services.[18,19] The reference unit prices of health care services for 2003 were adjusted to prices in 2005 by using the consumer price index.[20] The mean direct costs per 4 weeks were multiplied by 13 to calculate the annual costs.

The second part of the TiC-P includes a short form of the Health and Labor Questionnaire for collecting data on productivity losses.[21] The short form of the Health and Labor Questionnaire consists of 3 modules that measure productivity losses: absence from work, reduced

efficiency at work, and difficulties with job performance. The days of short-term absence from work and actual hours missed at work because of health-related problems were multiplied by the net income of the patient per day and per hour, respectively. The number of lost working days per patient was calculated, taking into account the number of days and hours of paid employment of the patient per week. The recall period for the short form of the Health and Labor Questionnaire is 2 weeks. Therefore, the mean indirect costs due to short-term absence were multiplied by 26 to calculate the annual costs. In order to assess long-term absence from work, patients who indicated to be absent from work longer than the preceding 2 weeks were asked when this period of absence started. To value long-term absence from work, we applied the friction-cost method. This method takes into account the economic circumstances that limit the losses of productivity to society, which is related to the fact that a formerly unemployed person may replace a person who becomes disabled.[22] The period needed to replace a worker (the so-called friction period) is estimated to be 5 months. Hence, the maximum indirect costs to society were confined to productivity losses during a period of 5 months.

Additionally, the TiC-P includes a list of 28 chronic medical disorders, e.g., rheumatic disease, diabetes, asthma, Parkinson's disease, migraine, cancer, and burnout/ severe tension. The patients were requested to indicate which of the chronic medical disorders they had experienced in the past year.

Personality disorders were assessed using the Dutch version[23] of the Structured Interview for DSM-IV Personality.[24] This instrument includes the 11 formal DSM-IV Axis II diagnoses (e.g., schizoid personality disorder) including personality disorder mixed, the 2 DSM-IV appendix diagnoses (depressive and negativistic personality disorder), and, in addition, the DSM-III-R self-defeating personality disorder. Personality disorder mixed is diagnosed when at least 10 diagnostic criteria are present, but no specific personality disorder is present. Interviewers were master-level psychologists, who were trained thoroughly by one of the authors (RV), and who received monthly booster sessions to avoid drift from the interviewer guidelines. Interrater reliability, based on 30 videotaped interviews rated by 3 observer-raters, was good. Percentage agreement ranged from 84% (avoidant personality disorder) to 100% (schizoid personality disorder) (median = 95%). Intraclass correlation coefficients for the sum of DSM-IV personality disorder traits present (i.e., scores of 2 or 3) ranged from 0.60 (schizotypal personality disorder) through 0.92 (antisocial personality disorder) (median = 0.74).

Statistical analysis

Univariate regression analyses were performed in order to compare the costs of each personality disorder type versus the patients without personality disorder.

The majority of patients (54.9%) were diagnosed with at least 2 personality disorder diagnoses. For that reason, multiple regression main effect analyses were conducted, measuring the unique contribution of the different diagnoses on the costs. In the analysis, a ranked definition of the presence of a diagnosis was used: no traits, only traits but no diagnosis, and the diagnosis present. An additional variable was entered into the multiple regression models to account for possible interactions between diagnoses. Because the number of possible interactions between the 14 independent variables becomes intractable, the interaction term is represented by a count of the diagnoses present. Age and gender variables are associated with health service use and were therefore entered into the regression models.[25]

Chronic medical disorders are expected to induce high costs due to elevated use of both mental and somatic health care and a high impact on productivity losses. Hence, an addi-

tional regression analysis was performed to control for medical disorders to ascertain the unique contribution on the variation in costs.

Results

Study participants

In the present sample of 1740 participants, depressive (31.8%), avoidant (28.3%), obsessive-compulsive (20.9%), and borderline (20.9%) personality disorders were the most frequently diagnosed disorders. Schizotypal (1.0%) and schizoid (1.1%) personality disorders were the least frequently diagnosed disorders (see Table 3.3). In 320 patients, no personality disorder could be diagnosed. As patients can be diagnosed with more than 1 diagnosis of personality disorder, the percentages will add up to more than 100%. The percentage of patients with a paying job was 53.7%. Of the patients without paying jobs, 68.1% indicated that they were unable to work because of health-related problems.

Table 3.1 Mean direct medical costs per year of patients with personality disorder (N = 1420)

Type of service	Cost (2005 prices), €	Percentage of total direct medical costs	Subjects using the service, N (%)
General practitioner	223.49	3.0	630 (44.4)
Company doctor	89.85	1.2	357 (25.1)
Physiotherapist	108.26	1.5	169 (11.9)
Alternative health practitioner	165.80	2.2	155 (10.9)
Domestic help	115.50	1.6	25 (1.8)
Self help group	69.52	0.9	42 (3.0)
Social worker	137.71	1.9	138 (9.7)
Substance abuse outpatient care	27.99	0.4	13 (0.9)
Ambulatory mental health care	1,933.33	26.1	642 (45.2)
Psychiatric practice	705.70	9.5	443 (31.2)
Out-patient psychiatrist (general hospital)	289.31	3.9	208 (14.6)
Out-patient psychiatrist (psychiatric hospital)	561.81	7.6	75 (5.3)
Inpatient health care (total):	2,451.54	33.1	58 (4.1)
Medical care	1,001.54	13.5	27(1.9)
Psychiatric care	1,450.00	19.6	32(2.3)
Medical specialist	110.70	1.5	143 (10.1)
Medication	407.33	5.5	945 (66.5)
Total	7,397.85		

Direct medical costs

Table 3.1 shows the mean direct medical costs per year differentiated by type of medical service incurred by the patient group with 1 or more personality disorders. The total mean direct medical costs per patient were €7,398 per year. These costs are mainly composed of costs due to inpatient health care (33.1%) (e.g., admissions into general or psychiatric hospital) and outpatient mental health care (26.1%). In a multiple regression analysis, paranoid ($p = .035$), borderline ($p = .011$), and obsessive-compulsive ($p = .028$) personality disorders were associated with increased direct medical costs.

Indirect costs

Table 3.2 presents indirect cost data for the group of patients with at least 1 personality disorder and a paying job. The total mean indirect cost per patient with a paying job was €7,088 per year. The total days lost because of absence from work or inefficiency at work was 47.6 per patient per year. In a multiple regression analysis, borderline ($p = .047$) and obsessive-compulsive ($p = .003$) personality disorders, age ($p < .001$), and gender ($p < .001$) were associated with increased indirect costs in patients with a paying job.

Table 3.2 Mean indirect costs per year of patients with a paying job and at least 1 personality disorder diagnosis (N = 743)

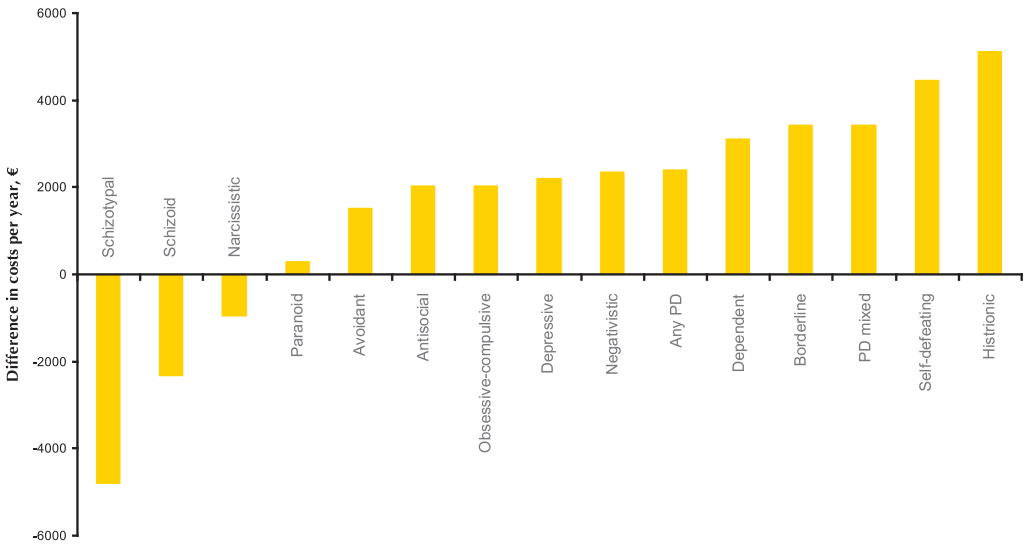
Type of indirect cost	Days	Cost (2005 prices), €
Absence from work	27.7	6,112.63
Reduced efficiency at work	19.9	959.88
Difficulties with nonpaying jobs	0.2	15.10
Total	47.8	7,087.61

Total costs of personality disorders

The mean total cost in the 12 months prior to treatment in the total group of patients with personality disorder was €11,126 (range, €0 to €147,759) per patient. The mean direct medical cost was €7,398 per year per person (66.5%), while a mean of €3,728 per patient (both with and without a job) was due to indirect costs.

In **Figure 3.1**, the results of the univariate analyses for each of the 14 personality disorder types are displayed. The graph shows that the majority of the personality disorder types induce higher mean costs compared to the patients without personality disorder, although the difference was statistically significant only for borderline (p = .021), histrionic (p = .050), self-defeating (p = .021), any personality disorder (p = .033), and personality disorder mixed (p = .030).

Figure 3.1. Difference in mean total costs (direct and indirect) of the personality disorder types compared to the patients without personality disorder



The main effects of the 14 personality disorder types, as studied in a multiple regression analysis, showed that borderline (p = .014) and obsessive-compulsive (p = .003) personality disorders had a unique contribution on the total costs. These results are summarized in **Table 3.3**. As patients can have more than 1 personality disorder, the sum of the number of patients in the different diagnostic groups is higher than the total number of patients included in this study. In the regression model also, the age variable, which is directly influencing the indirect costs, significantly predicted total costs (p = .030). The total number of personality disorders diagnosed, representing an additional interaction effect, did not have an independent effect on the total costs. The maximum variance of total costs that was explained by these variables (age, gender, 14 diagnoses of personality disorders, number of diagnoses) in the regression model was 2.4%.

Table 3.3 Multivariate predictors of total costs (direct and indirect) of patients with personality disorder, €

Multivariate predictor	N	ß [a]	SE	p value
Constant [b]	NA	952.11	3370.02	.778
Gender	NA	-940.64	1015.59	.354
Age	NA	102.36	47.07	.030
Paranoid	106	-1111.98	680.19	.102
Schizoid	20	-381.70	687.58	.579
Schizotypal	17	-165.09	828.52	.842
Antisocial	36	-540.12	652.49	.408
Borderline	364	1962.27	794.93	.014
Histrionic	51	75.39	671.39	.911
Narcissistic	103	-1229.69	690.69	.075
Avoidant	492	-694.47	759.60	.361
Dependent	182	1231.22	716.84	.086
Obsessive-compulsive	363	2184.02	741.43	.003
Self-defeating	118	14.04	730.31	.985
Depressive	553	1735.30	1029.92	.092
Negativistic	64	-719.64	681.48	.291
Personality disorder mixed	262	839.92	1062.07	.429
Number of diagnoses	NA	18.24	394.59	.963

a For continuous variables (e.g., age), the coefficient indicates the increase or decrease in cost per unit increase in the covariate (e.g., per year of age). For categorical variables, the coefficient is the difference in cost between the specified group and the comparison group. For the diagnoses, 3 categories are specified: no traits; only traits, no diagnosis; and presence of the diagnosis. Adjusted R^2=0.024.

b Refers to the constant in the regression equation, also referred to as the intercept.

Abbreviation: NA = not applicable.

When studying the main effects of the chronic medical disorders in a multiple regression analysis, 3 out of 28 appeared significant, indicating that having that specific medical condition has a significant effect on the total costs in this sample. These medical conditions are kidney stones, burnout/severe tension, and injury by accident. Adjusting the original multiple regression model by entering these 3 variables showed that in addition to age ($p = .047$), kidney stones ($p < .001$), burnout/severe tension ($p = .035$), and injury by accident ($p = .006$), borderline ($p = .026$), and obsessive-compulsive ($p = .005$) personality disorders were significant predictors of the total costs. The proportion of explained variance of total costs in the regression model was 4.3%.

The cost data in the present study are nonnormally distributed, due to a majority of patients with roughly similar costs and only a small proportion of patients who induce very high costs. Cost data are typically found to be positively skewed. Log transformations are often used to solve the problems of the violation of assumptions (nonnormality and heteroscedasticity of the residuals) of multivariate linear regression analysis. Concordantly, we performed a log trans-

formation on the dependent cost variable. The log-transformed model remains significant for borderline personality disorder (p = .007), obsessive-compulsive personality disorder (p = .026), and age (p = .003). The R square, although higher compared to the nontransformed model, is still relatively small (3.1%). This indicates that the small R square in the nontransformed model was not due to the violation of the normality assumption.

Discussion

In summary, treatment-seeking patients with personality disorders are accountable for high costs to society. The most relevant cost drivers were absence from work, inpatient health care, and outpatient mental health care. In this sample of 1740 adults, borderline and obsessive-compulsive personality disorders were uniquely associated with increased mean total costs. This conclusion holds even after controlling for chronic medical disorders. Compared to the patients without personality disorder, mean total costs were consistently higher for borderline, histrionic, and self-defeating personality disorder, any personality disorder, and personality disorder mixed. Although not statistically significant, mean total costs were least in schizotypal and schizoid personality disorder as compared to the group without personality disorder. This finding can mainly be attributed to relatively low costs due to absence from work in both personality disorder groups. Additionally, in schizotypal personality disorder, the percentage of employment was considerably lower compared to the group without personality disorder.

We found that the amount of direct medical costs, and thus the usage or volumes of these medical services, is associated with some of the personality disorder types (paranoid, borderline, and obsessive-compulsive). This finding seems in part consistent with the study of Bender and colleagues.[7] They also reported that patients with certain types of personality disorders received treatments more often than those with other personality disorders. Borderline personality disorder was found to receive greater amounts of psychosocial treatments (i.e., individual and group psychotherapy, day treatment, psychiatric hospitalization, and halfway house residence) than the other personality disorder groups (schizotypal, avoidant, and obsessive-compulsive). The differences in results between the 2 studies might be explained by the fact that the Bender study includes only 4 diagnoses of personality disorders and that the 4 personality disorder types could not be comorbid with each other.

The economic burden of personality disorders seems considerably higher than the burden of patients seeking mental health treatment for other mental disorders, such as depression and generalized anxiety disorder, and comparable to that in schizophrenia. (For reasons of comparison, all costs were converted to Euros by using the mean exchange rate for 2006 of 1€ = $1.33 U.S. and 1€ = £0.68 U.K.) A systematic review of cost-of-illness studies of depression[6] found that the average annual costs per case ranged from €752 to €1,880 for direct costs and from €1,654 to €3,083 for indirect costs depending on international differences. In another review, the total costs (direct and indirect) of generalized anxiety disorder patients in ambulatory care (with comorbidity) were reported to be €3,634 per year and patient.[26] In a study on service utilization in schizophrenic patients in contact with mental health services in 5 European countries, average direct costs were calculated of €7,419 per annum and patient.[3]

In the current study the direct medical costs clearly exceed (66.5%) the indirect costs of productivity losses. In most literature on mental and chronic diseases, the opposite is observed: indirect costs constitute the major part of the total costs. This is because virtually all studies used

the human capital approach.[27] The human capital approach has been criticized as calculating potential rather than actual productivity costs, leading to unrealistically high estimates of productivity costs.[28] By using the friction cost method as an alternative to the traditional human capital approach, we used the most conservative method in estimating costs of productivity losses. Moreover, we believe that the societal perspective or the actual loss for society is represented best in this friction cost method. In the case of long-term absence from work, the friction cost method limits costs to a friction period, the time needed to replace a worker, whereas the human capital approach estimates the indirect costs as the value of the productivity loss from the age of disablement of the person until the age of retirement or until the time the person has found an equivalent job. However, in our case no long-term follow-up data on personality disorder patients regaining employment are available. Therefore, when we used the human capital method in our study, we had to make the assumption that the productivity losses would last until the age of retirement. Research comparing the friction cost method with the human capital approach has shown a major influence of the methods used. For example, in a study on the productivity costs among patients with rheumatic arthritis, researchers found that the productivity costs were 15 times higher when using the human capital approach instead of the friction cost method.[29] Furthermore, a comparison of the 2 methods for schizophrenia showed productivity costs that were even 69 times higher by using the human capital approach.[30]

The 1740 participants included in this study were recruited from 6 different mental health care institutes in the Netherlands specializing in the psychotherapeutic treatment of personality problems and disorders. The large number of patients and the different settings can be considered one of the strengths of this study, as these enhance the external validity of the results. On the other hand, we only sampled patients that were referred to psychotherapeutic treatments; therefore, the results may not be generalizable to all prevalent cases in the community.

Moreover, the patients in our sample can be considered treatment-seeking patients, i.e., they have the wish to receive treatment, as opposed to treatment-rejecting patients. This distinguishing feature of personality disorders mentioned in literature[31] may affect the outcome. For future research it would be interesting to study direct and indirect costs in both treatment-seeking and treatment-rejecting personality disorder patients, e.g., in forensic care or in the normal population.

Another limitation of our study is that no standardized diagnoses of comorbid Axis I disorders were available, e.g., mood disorders or substance use disorders. Note, however, that this limitation does not jeopardize the main findings of our study, which is that personality disorder patients who seek treatment pose a substantial economic burden on society. Among personality disorder patients admitting to a mental health care facility, it is difficult to find patients with "only" Axis II problems. Isolating the effects of the Axis I disorders would be the same as considering the economic burden of diabetes without the accompanying foot ulcers. The independent contribution of Axis I and Axis II pathology to costs parameters should be addressed in future research.

Despite evidence that prison service costs in personality disorders are high,[9] these costs were not included in the present study. This can be considered a limitation of the study as it leads to an underestimation of the direct cost calculations.

The recall periods for the use of medical services and short-term absence from work were 4 and 2 weeks, respectively. The annualization of these costs is based on the assumption that these 4 weeks (or 2 weeks) are representative for the rest of the year. In order to test this as-

sumption, an additional form was administered on which patients had to indicate the amount of outpatient, day-hospital, or inpatient psychological treatment they had received in the year prior to filling out the form. The utilization of outpatient, day-hospital, and inpatient care indicated on this form was then compared against the TiC-P, with a recall period of 4 weeks. The data indicated that on a population level there was no significant difference between the costs as measured with a recall period of a year (€3,440) compared to a recall period of 4 weeks (€3,247). Concordantly, there is no reason to believe that the costs calculated in the present study were an over/underestimation, but on the contrary are a realistic representation of the actual costs generated by this population in the year prior to treatment.

Given the fact that the unit cost prices used in the present study were, at least to some extent, subject to uncertainty, one should consider testing the robustness of the results to changes in unit prices. We acknowledge that this study is based on the assumption of a certainty in the unit costs that may not be there. However, the expectation is that unit prices are not of much influence on the outcome, as they are constants.

Borderline personality disorder has traditionally attracted much scientific and clinical attention,[32] which also has affected the prominent research concerning the utilization of health care resources and productivity losses. Although in our study only borderline and obsessive-compulsive personality disorders were found to have a unique contribution on the costs, this result does not mean that the high societal costs of the other personality disorder types can be ignored. We thus argue that, from a health economic perspective, research should also focus on the other personality disorder types instead of primarily on borderline personality disorder.

It is important to emphasize that, although cost-of-illness studies such as this do provide valuable information for the policymaker, these findings do not provide any information on the effectiveness of available treatment programs. Therefore, in order to fully appreciate the value of a treatment program, health care policymakers should be informed with state-of-the-art cost-effectiveness analyses. Accordingly, the present cost-of-illness study is incorporated into a large cost-effectiveness study that compares different modalities of psychotherapy (outpatient, day-hospital, and inpatient) in treating personality disorders. Results of this cost-effectiveness analyses will become available in 2009.

In the mean time, our results provide evidence that the economic burden of personality disorders is high; higher than, for instance, that of depression and generalized anxiety disorder. These high societal costs, in combination with a low quality of life that was found in earlier research,[33] reflect the severity of illness and thus present a strong argument in favor of prioritizing effective personality disorder treatments in reimbursement decisions.

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Cost-Effectiveness of Psychotherapy for Cluster C Personality Disorders

Chapter 4

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Abstract

Objective

To conduct a formal economic evaluation of various dosages of psychotherapy for patients with avoidant, dependent, and obsessive-compulsive (i.e., cluster C) personality disorders (PD).

Method

We developed a decision-analytic model to assess the cost-effectiveness of five dosages of psychotherapy (i.e., long-term outpatient psychotherapy, short-term and long-term day hospital psychotherapy, and short-term and long-term inpatient psychotherapy) over a five-year time horizon in terms of cost per recovered patient-year and cost per quality-adjusted life year (QALY). Model parameters were estimated using data from 466 patients with cluster C PD who were admitted to six specialist centers of psychotherapy in the Netherlands and assigned to one of the five treatment groups. Probabilistic analysis was conducted to explore the stability of results over uncertain data ranges. Analyses were conducted from both societal and payer perspectives.

Results

From the societal perspective and below a threshold of €2,637 per recovered patient-year, short-term day hospital psychotherapy resulted in the highest level of benefit for its cost; above the threshold, short-term inpatient psychotherapy was the most cost-effective choice. In terms of cost per QALY, this switch point was at a threshold value of €16,570 per QALY. From the payer perspective, the optimal strategy changed from short-term day hospital psychotherapy to short-term inpatient psychotherapy at threshold values of €9,874 per recovered patient-year and €66,302 per QALY.

Conclusion

This study indicates that short-term day hospital psychotherapy and short-term inpatient psychotherapy are the most cost-effective treatment strategies for patients with cluster C PD. The ultimate selection depends on what cost-effectiveness threshold is considered acceptable and what perspective is adopted.

Introduction

Cluster C personality disorders (PD), including avoidant, dependent, and obsessive-compulsive PD, are among the most common mental disorders in the general population with reported prevalence rates of 6.0-9.4 percent.[1,2] Moreover, these disorders are associated with high societal costs and a low quality of life.[3,4,5] Recently, a multidisciplinary clinical guideline of PD, summarizing the evidence from over 100 effectiveness studies, was published in The Netherlands. In this guideline, various modalities of psychotherapy, including outpatient, day hospital, and inpatient psychotherapy, were considered treatments of choice for cluster C PD based on strong evidence of efficacy.[6,7] However, the economic impact of these recommendations has not yet been explored.

In a budget-constrained health care system there is a clear need to search for the most cost-effective treatment option. Despite the high economic burden of PD, little quantitative economic information is available that can guide decision making with respect to clinical practices and health care resource allocations. Recently, the Study on Cost-Effectiveness of Personality disorder Treatment (SCEPTRE) was designed to conduct an economic evaluation of various psychotherapeutic treatments for PD. Patient-level primary data was available from the largest existing clinical trial of psychotherapy for PD,[8] including over 900 patients that were followed for three years.

The objective of this study is to evaluate the cost-effectiveness of five dosages of psychotherapy in treating cluster C PD (i.e., long-term outpatient psychotherapy, short-term and long-term day hospital psychotherapy, and short-term and long-term inpatient psychotherapy). We incorporated clinical and economic patient-level data from the SCEPTRE trial in a decision-analytic model to compare the strategies over a five-year time horizon in terms of costs per recovered patient-year and costs per quality-adjusted life year (QALY). The decision analysis framework recognizes the need to make decisions on the basis of currently available evidence, even if that information is imperfect, and facilitates exploration of the uncertainty surrounding the decisions.[9] The findings from our study can be used to inform decision makers about the value for the cost of current treatment options for PD.

Methods

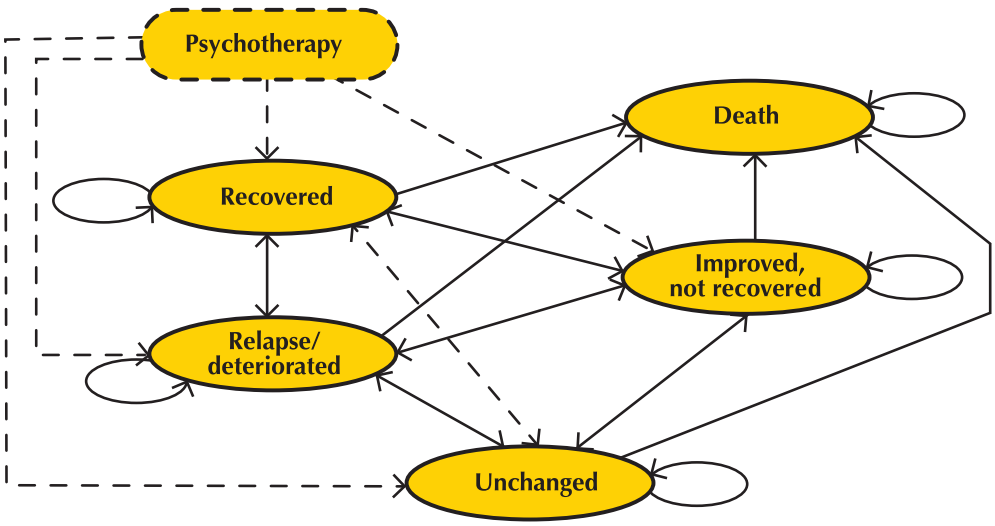
Model

We developed a Markov cohort model[9] to integrate clinical and economic data from the SCEPTRE trial. In general, the model comprises of mutually-exclusive and collectively exhaustive health states that represent knowable prognoses of a health condition. The Markov model simulates a cohort of patients that transition through the model over time, based on data from epidemiological and clinical studies, and estimates the impact of different interventions on the patient population. The underlying clinical process driving the current model and by which the health states are defined is 'clinically significant change', based on a statistical approach to defining meaningful change in psychotherapy research.[10] Patients are classified into one of four health states: (1) recovered (if the magnitude of change is statistically reliable and the patient ends up within normal limits on the variable of interest), (2) improved (if the patient shows statistically reliable change but ends therapy still somewhat dysfunctional), (3) unchanged (if the magnitude of change is not statistically reliable, the method cannot determine whether or not the change is clinically significant), and (4) relapsed or deteriorated (if a statistically reliable change

is in the opposite direction to that indicative of improvement). At anytime, patients can also die from suicide or age-specific background mortality. The structure of the Markov model is shown in **Figure 4.1**.

Four types of parameters were used in the model: (1) transition probabilities, which govern the movement between the five states at each cycle, (2) treatment costs of the five dosages of psychotherapy, (3) costs of health care utilization and productivity losses incurred by patients in each state, and (4) health state utilities, which reflect the health-related quality of life experienced by patients in each state. These data were obtained from a single patient-level data source (i.e., the SCEPTRE trial). A nonrandomized clinical trial design was chosen to optimize feasibility and external validity. Naturalistic trials have several advantages for economic evaluation and accordingly have a high status.[11,12] To overcome the problem of selection bias, we controlled for initial differences in patient characteristics with the propensity score method (see below). The results are based on intention-to-treat analyses.

Figure 4.1 State transition diagram of the Markov model for psychotherapy



Transitions between health states in the model occur over time at a constant interval that was assumed to be six months, corresponding to multiple changes in pathology, symptoms, treatment decisions, or costs for patients with PD. The time horizon of the analysis was five years, which is the duration of the clinical trial expanded by two years. Costs per recovered patient-year and costs per quality-adjusted life year (QALY) were estimated over the five years using the model; costs and QALYs were discounted at an annual rate of 4.0% and 1.5% respectively, consistent with guidelines for economic evaluations in the Netherlands.[13] The base case analysis was conducted from the societal perspective, and a secondary analysis from the payer perspective.

Recruitment and assignment

Patients were recruited from a consecutive series of admissions to six mental health care institutes in the Netherlands offering specialized psychotherapy for adult patients with PD. Diagnoses were based on the Dutch version[14] of the Structured Interview for DSM-IV Personality (SIDP-IV).[15] Interrater reliability was good.[3] For this particular study, inclusion criteria were a diagnosis of cluster C PD, age 18 to 70 years, assignment to a specified dosage of psychotherapeutic treatment for PD, and Dutch literacy. Exclusion criteria were psychotic disorders (e.g. schizophrenia), organic cerebral impairment, and mental retardation. Comorbid Axis I and Axis II disorders were allowed.

From March 2003 to March 2006, 1379 individuals completed the intake procedure and were selected for various treatment options. Of those, 466 patients were eligible, provided informed consent, and entered the study.

The treatments in the six institutes differ widely in terms of setting, duration, intensity, theoretical framework, and therapeutic techniques. This study compares dosage, specified by a combination of treatment setting (outpatient, day hospital, and inpatient) and duration (short-term or up to six months versus long-term or more than six months).

Patients were assigned to one of six treatment groups, based on a comprehensive assessment battery combined with the expert opinion of clinicians. Only a few patients with cluster C PD were assigned to short-term outpatient psychotherapy (n=18). Therefore, and because this particular dosage is not recommended in clinical guidelines, this option was excluded from the study. Thus, the treatments under study were long-term outpatient psychotherapy, short-term and long-term day hospital psychotherapy, and short-term and long-term inpatient psychotherapy.

In the long-term outpatient strategy, patients are offered up to two sessions per week of individual or group psychotherapy for more than six months. In the short-term day hospital strategy, patients are offered psychotherapy combined with sociotherapy and/or non-verbal therapies for one to five days per week for up to six months. In the long-term day hospital strategy, patients are offered the same for more than six months. The inpatient strategy also offers psychotherapy combined with sociotherapy and/or non-verbal therapies, but patients reside in the treatment centers five days per week. The therapists were licensed psychiatrists or psychologists. On average, they had 14.9 years (SD=10.1) of postgraduate clinical experience. See **Table 4.1** for an overview of demographic, clinical, and treatment characteristics of the study participants in each treatment group.

Input data

Transition probabilities – The percentage of patients in the recovered, improved, unchanged, and relapsed or deteriorated health states was determined at 6, 12, 24, 36, and 42 months after baseline from the SCEPTRE trial. Based on the difference between the frequency distributions over time, the probabilities of transitioning from one state to another in each time period were calculated. The one-year probabilities i.e., between 12-24 and 24-36 months, were first converted to rates and then to six months probabilities.[9] Several methods of extrapolating the transition probabilities were considered to fit the five year time horizon of the model. Based on the best fit to the data, we elected to average the last two observations from the trial and hold those values constant over the last one and a half year of the analysis. Transition probabilities over time are provided in **Appendix A**.

Table 4.1 Demographic, clinical, and treatment characteristics of 448 study participants

Psychotherapy dosage	Long-term outpatient	Short-term day hospital	Long-term day hospital	Short-term inpatient	Long-term inpatient
	(n=96)	(n=85)	(n=103)	(n=63)	(n=101)
Age, mean (SD), year	36.2 (9.0)	35.0 (9.5)	31.9 (9.7)	37.6 (9.3)	28.4 (6.6)
Sex %					
Female	66.7	77.6	75.7	61.9	65.3
Comorbidity Axis II %					
pure cluster C					
(no comorbid cluster A/B)	60.4	65.9	61.2	85.7	63.4
cluster C and cluster B	27.1	27.1	21.4	9.5	27.7
cluster C and cluster A	7.3	2.4	4.9	1.6	4.0
cluster C and both					
cluster A and B	5.2	4.7	12.6	3.2	5.0
Personality disorder %					
avoidant	53.1	52.9	67.0	66.7	73.3
obsessive-compulsive	58.3	52.9	42.7	46.0	40.6
dependent	13.5	28.2	28.2	17.5	26.7
Treatment characteristics, mean (SD)					
duration, months	15.5 (6.4)	5.4 (1.3)	12.1 (2.6)	4.3 (1.5)	10.2 (2.0)
# sessions or days/week	0.8 (0.5)	3.2 (1.5)	3.3 (1.4)	5	5

Costs – Costs were estimated from both societal and payer perspectives. The calculations from the societal perspective included direct medical costs (i.e., primary treatment costs and costs of health care utilization post-discharge) and direct non-medical costs (i.e., lost productivity due to time spent in treatment), as well as indirect costs (i.e., future lost productivity due to disease), while the payer perspective included only direct medical costs. Mean primary treatment costs for the five strategies were calculated by multiplying the resource quantities with the 2007 unit costs or prices of the corresponding treatment options. We obtained data from the hospital finance departments on staff salaries, equipment, buildings and departmental overheads, and used a micro-costing approach to derive the cost of a treatment session and an inpatient day. The resource quantities were collected from the hospital data systems. Costs due to productivity loss because of patients' time in treatment were also estimated and included in the analysis from the societal perspective. The mean (SE) treatment costs were €10,005 (1,134) for long-term outpatient psychotherapy, €16,813 (1,361) for short-term day hospital psychotherapy, €27,648 (2,654) for long-term day hospital psychotherapy, €25,933 (859) for short-term inpatient psychotherapy, and €49,260 (2,435) for long-term inpatient psychotherapy.

Post-discharge costs due to health care utilization and productivity losses may still be substantial; therefore, we assigned a cost to each health state. The Trimbos and Institute for Medical Technology Assessment (iMTA) Questionnaire on Costs Associated with Psychiatric Illness (TiC-P) was used to collect data on direct medical and indirect costs.[16] Bottom-up methodology was used to calculate the direct medical costs; for example, the total number of medical visits (e.g., outpatient visits, hospital lengths of stay, use of medication) was multiplied by the 2003

unit prices of the corresponding health care services.[17,18] The reference unit prices of health care services for 2003 were adjusted to prices in 2007 using the consumer price index.[19] The mean direct medical costs per four weeks were multiplied by 6.5 to calculate the half-yearly costs to correspond to the model cycle length. In addition, the TiC-P includes a short form of the Health and Labor Questionnaire consisting of three modules that measure indirect costs: absence from work, reduced efficiency at work, and difficulties with job performance.[20] The days of short-term absence from work and actual hours missed at work because of health-related problems were multiplied by the net income of the patient per day and per hour, respectively. The number of lost working days per patient was calculated, taking into account the number of days and hours of paid employment of the patient per week. To value long-term absence from work, we applied the friction-cost method. This method takes into account the economic circumstances that limit the losses of productivity to society, which is related to the fact that a formerly unemployed person may replace a person who becomes disabled.[21] The period needed to replace a worker (the so-called friction period) is estimated to be five months. Hence, the maximum indirect costs to society were confined to productivity losses during a period of five months. The mean costs associated with spending six months in each health state are summarized in **Table 4.2**. To reflect the change in costs over time, we further delineated these data by number of years in the model. For each strategy, the model calculates the expected cost by taking a weighted average of the costs of each health state and the proportion of the cohort in each health state at each six-month period; the total expected cost of the strategy is then calculated by summing over the five year time horizon.

Health utilities – To reflect the diminished quality of life of patients with PD, health utility weights were assigned to each health state, using the EuroQol EQ-5D.[22] The descriptive system of the EQ-5D records quality of life in five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into three response levels: no problems, some or moderate problems, and extreme problems or complete inability. The combination of scores makes up a total of 243 different possible health states, each weighted to arrive at a single index score between –0.33 (worst imaginable health state) and 1.00 (best imaginable health state). The Dutch norm scores were used for calculating the mean EQ-5D index values.[23] The mean quality of life utilities of a year spent in each of the model health states for each cycle are summarized in **Table 4.2**. The expected number of QALYs for each strategy was estimated by weighing the duration of time in a particular health state by the utility of that health state and then summing over all health states in each cycle. The expected number of QALYs per patient over five years was calculated by summing over all cycles.

Mortality rates – In our model we assumed that patients in the recovered health state had a risk of death equivalent to that observed in the general population. These age- and sex-specific mortality rates were obtained from standard life tables.[24] Moreover, we assumed patients in the improved, unchanged and relapsed or deteriorated health states faced an elevated risk of death due to suicide, estimated to be a half-yearly probability of 0.00127 based on the SCEPTRE data.

Table 4.2 Values for model input parameters: health state costs and utilities over time from the societal perspective

Health states		Recovered	Improved	Unchanged	Relapsed or det.
Health state costs [a], mean (SE)					
years	1 to 2	€ 6,714 (2,257)	€ 15,287 (5,126)	€ 7,836 (1,913)	€ 42,526 (12,866)
	3	€ 3,390 (818)	€ 6,754 (2,801)	€ 4,474 (934)	€ 13,753 (6,818)
	4 to 5	€1,903 (304)	€ 6,284 (3,377)	€ 6,852 (1,562)	€ 15,229 (9,092)
Health utilities [b], mean (SE)					
years	0.5	0.87 (0.02)	0.76 (0.09)	0.69 (0.13)	0.43 (0.09)
	1.0	0.84 (0.03)	0.72 (0.04)	0.70 (0.03)	0.43 (0.09)
	1.5	0.82 (0.02)	0.69 (0.03)	0.67 (0.02)	0.52 (0.06)
	2.0	0.84 (0.02)	0.64 (0.04)	0.70 (0.03)	0.42 (0.09)
	2.5	0.83 (0.02)	0.67 (0.04)	0.72 (0.02)	0.61 (0.07)
	3.0	0.88 (0.02)	0.55 (0.08)	0.63 (0.06)	0.53 (0.28)
	4 to 5	0.86 (0.01)	0.67 (0.04)	0.70 (0.02)	0.16 (0.06)

a Mean cost estimates of a half year spent in each of the model health states. Estimates include post-discharge costs due to health care utilization and productivity losses. As costs may vary according to time in model we calculated different cost estimates for the first two years, third, and last two years in the model.

b Mean quality of life utilities of a year spent in each of the model health states. In the model the reported utility weights were divided by two to fit the half-yearly cycle. As quality of life may vary according to time in model we calculated different utility weights for time intervals of six months until year three. For the last two years in the model a constant utility weight was used.

Propensity score method

To overcome the problem of selection bias, we controlled for initial differences in patient characteristics with the multiple propensity score method.[25] The estimated propensity score is defined as the conditional probability of assignment to a particular treatment, given a set of observed pre-treatment characteristics. Details of the method and the variables used to estimate the propensity scores are described elsewhere.[8,26] Multinomial regression analyses were conducted to adjust the transition probabilities for the multiple propensity scores.

Probabilistic sensitivity analysis

In order to explore the impact of uncertainty across multiple parameters simultaneously, we conducted a probabilistic analysis in which distributions were assigned to the input parameters of the model i.e., gamma distributions for costs, and beta distributions for utilities. We assumed probability parameters followed a Dirichlet distribution, a continuous distribution that is the multivariate generalization of the beta distribution.[9] These distributions reflect the characteristics of the type of parameter and its method of estimation (e.g., probabilities are bound by the values of zero and one, and cost data are often highly skewed). The probabilistic analysis was undertaken by randomly sampling from each of the parameter distributions and calculating

the expected costs, expected recovery rate, and QALY for each strategy using that combination of parameter values in the model. This process was replicated one thousand times (i.e., second-order Monte Carlo simulation) for each treatment option and represented on a cost-effectiveness plane. The outcomes projected from all 1000 simulations were used in the cost-effectiveness analysis.

Cost-effectiveness analysis

We compared the five psychotherapy dosage strategies by conducting a cost-effectiveness analysis. Strategies that were more costly and less effective than an alternative option were considered sub-optimal (i.e., strongly dominated) and were therefore eliminated from the final cost-effectiveness calculations. For the remaining strategies, the incremental cost-effectiveness ratio (ICER) was calculated as the additional cost divided by the additional health benefit of the treatment, compared with the next best non-dominated treatment. The mean values of costs and QALYs across all 1000 simulations were used to calculate the ICER associated with each strategy. The most cost-effective strategy was then identified by comparing the ICERs of different strategies against various threshold values, which reflect the decision maker's willingness to pay (WTP) for an additional unit of effect. Strategies below a specific WTP value generally represent good value for money; the "most cost-effective" strategy is the strategy with the highest ICER below the WTP threshold, representing the option that yields the highest level of benefit for its cost.

In order to reflect the uncertainty in the parameter values, cost-effectiveness acceptability curves (CEAC) were created to indicate the probability of each option being cost-effective conditional on the decision maker's WTP for a recovered patient-year or QALY.[27] The curve summarizes the proportion of simulations in which strategies are identified as being cost-effective at different potential WTP threshold values. Finally, the cost-effectiveness acceptability frontier (CEAF) was plotted to portray each CEAC over the range of threshold values for which each option is estimated to be the most cost-effective, as well as the threshold ICER at which there are changes in the optimal dosage (i.e., "switch points").[28]

Results

One-year and five-year costs and health outcomes

The mean one-year and five-year costs and health outcomes from the societal perspective are presented in **Table 4.3**. The table shows that the treatment options differ widely in both costs and health outcomes at one year, while these differences tend to become less pronounced over time. Short-term inpatient psychotherapy stands out as the most effective option at one year, and long-term outpatient psychotherapy appears to be the least effective option at both time points. Despite differences in treatment costs, long-term outpatient psychotherapy, short-term day hospital psychotherapy and short-term inpatient psychotherapy are associated with similar overall costs at both time points. Furthermore, the costs associated with these three treatments are substantially lower than with long-term day hospital psychotherapy and long-term inpatient psychotherapy.

Table 4.3 Discounted costs and health outcomes over one and five years from the societal perspective

	one year			five years		
Psychotherapy dosage	**costs [a]**	**% recovered [b]**	**QALYs [c]**	**costs [a]**	**% recovered [b]**	**QALYs [c]**
Short-term day hospital	€ 40,070	26.0	0.70	€ 89,411	46.8	3.44
Long-term outpatient	€ 36,766	19.2	0.69	€ 89,936	31.3	3.30
Short-term inpatient	€ 44,460	60.9	0.78	€ 91,620	49.0	3.57
Long-term day hospital	€ 56,772	37.1	0.71	€ 105,940	49.8	3.49
Long-term inpatient	€ 73,456	40.8	0.73	€ 119,946	43.7	3.49

a Values represent mean cumulative costs per patient, including treatment costs and costs involved with spending time in each of the model health states.

b Percentage of patients resided in the recovered health state.

c Mean number of QALYs gained per patient. For someone spending their time in perfect health, the maximum amount of QALYs would have been 1.0 at one year and 5.0 at five years. For the current model this will be slightly lower, as the most optimal health state (recovered) is assigned a utility weight of 0.82-0.88 over time.

Cost-effectiveness analysis from the societal perspective

The cost-effectiveness analysis over a five-year time horizon is displayed in **Table 4.4**. The values represent the incremental cost-effectiveness ratio (ICER) expressed as cost per recovered patient-year and cost per QALY. Long-term day hospital psychotherapy and long-term inpatient psychotherapy were strongly dominated (i.e., more costly and less effective) by short-term inpatient psychotherapy, and thus eliminated. Long-term outpatient psychotherapy was dominated by short-term day hospital psychotherapy and thus had to be eliminated, however differences in costs between these strategies were small. Of the remaining treatment strategies, short-term day hospital psychotherapy yields the lowest costs and health benefits; short-term inpatient psychotherapy yields higher costs and effects and was associated with an ICER of €2,637 per recovered patient-year and an ICER of €16,570 per QALY compared to short-term day hospital psychotherapy.

To explore the uncertainty in model parameter values, we conducted a probabilistic analysis and plotted the relationship between cost and health outcomes for each of the five competing psychotherapy dosages over 1000 simulations in the cost-effectiveness plane (**Appendix B**). We found substantial uncertainty about both costs and effects for all treatment options; however the uncertainty around the effects was greater when health outcomes were expressed in terms of recovered patient-years (panel A) as opposed to QALYs (panel B). Furthermore, the observed differences in health effects among the five treatment strategies were more pronounced in terms of recovered patient-years than QALYs.

Figure 4.2 shows the cost-effectiveness acceptability curves (CEAC) representing the probability of each option being cost-effective at different values of the societal willingness-to-pay (WTP) for a unit of health benefit. In terms of both cost per recovered patient-year and cost per QALY, short-term inpatient psychotherapy has the highest probability of being cost-effective independent of the value of the societal WTP, whereas long-term day hospital psychotherapy and long-term inpatient psychotherapy have a negligible probability of being cost-effective. The CEAC crosses the Y-axis at the probability that the intervention under evaluation is cost-saving.[29] According to the current analysis, three dosages (i.e., short-term day hospital psychotherapy, short-term inpatient psychotherapy, and long-term outpatient psychotherapy) have a probability

of being cost-saving in approximately one third of the cases.

However, the probability of a strategy being cost-effective is not sufficient to determine the optimal option. If the societal objective is to maximize health gain, then decisions should be made on the basis of expected net benefit, regardless of the uncertainty (probability) associated with the decision.[27] To identify the optimal treatment option, (i.e. the option with the highest expected net benefit for a given cost), the cost-effectiveness acceptability frontiers (CEAF) were plotted (**Figure 4.3**). The CEAF of cost per recovered patient-year shows the range of threshold values over which short-term day hospital psychotherapy (€0 to €2,637) and short-term inpatient psychotherapy (above €2,637) have the highest expected net benefit and can be considered the optimal choice. The switch point, at which there is a change in the optimal option, correspond to the ICER between short-term day hospital and short-term inpatient psychotherapy. In terms of costs per QALY, the switch point was located at a threshold value of €16,570. If society's willingness-to-pay for a QALY is below this threshold short-term day hospital is the most cost-effective choice; above this value, the optimal strategy would be short-term inpatient psychotherapy.

Table 4.4 Cost-effectiveness analysis over a five-year time horizon

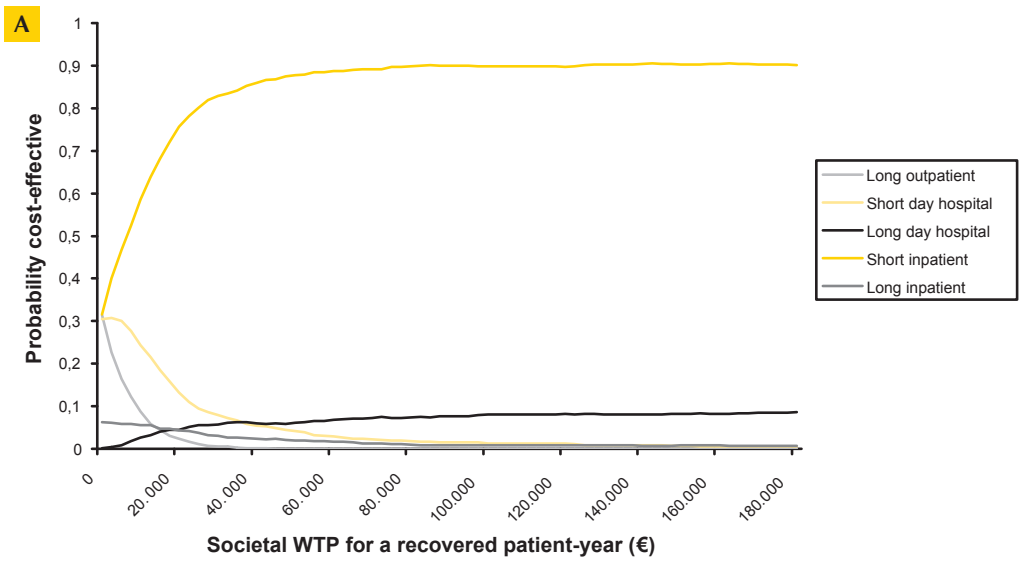
Societal perspective		
Psychotherapy dosage	**Cost per recovered patient-year**	**Cost per QALY**
Short-term day hospital	— [b]	— [b]
Long-term outpatient	strongly dominated[a]	strongly dominated[a]
Short-term inpatient	€ 2,637[c]	€ 16,570[c]
Long-term day hospital	strongly dominated[a]	strongly dominated[a]
Long-term inpatient	strongly dominated[a]	strongly dominated[a]
Payer perspective		
Psychotherapy dosage	**Cost per recovered patient-year**	**Cost per QALY**
Short-term day hospital	— [b]	— [b]
Long-term outpatient	strongly dominated[a]	strongly dominated[a]
Short-term inpatient	€ 9,874[c]	€ 66,302[c]
Long-term day hospital	strongly dominated[a]	strongly dominated[a]
Long-term inpatient	strongly dominated[a]	strongly dominated[a]

a These strategies are more costly and less effective than an alternative strategy, and are thus considered dominated.

b This strategy is non-dominated and considered the comparison group in the ICER mentioned.

c This strategy is more effective than short-term day hospital psychotherapy, but also more costly. The values represent incremental cost-effectiveness ratios (ICER) calculated as the difference in cost divided by the difference in quality-adjusted life years or recovered patient-years between the strategy (short-term inpatient psychotherapy) and the next best non-dominated strategy (short-term day hospital psychotherapy).

Figure 4.2 Cost-effectiveness acceptability curves (CEAC) showing the probability of each option being cost-effective at different values of the societal WTP. A, CEAC for recovered patient-year. B, CEAC for QALY.



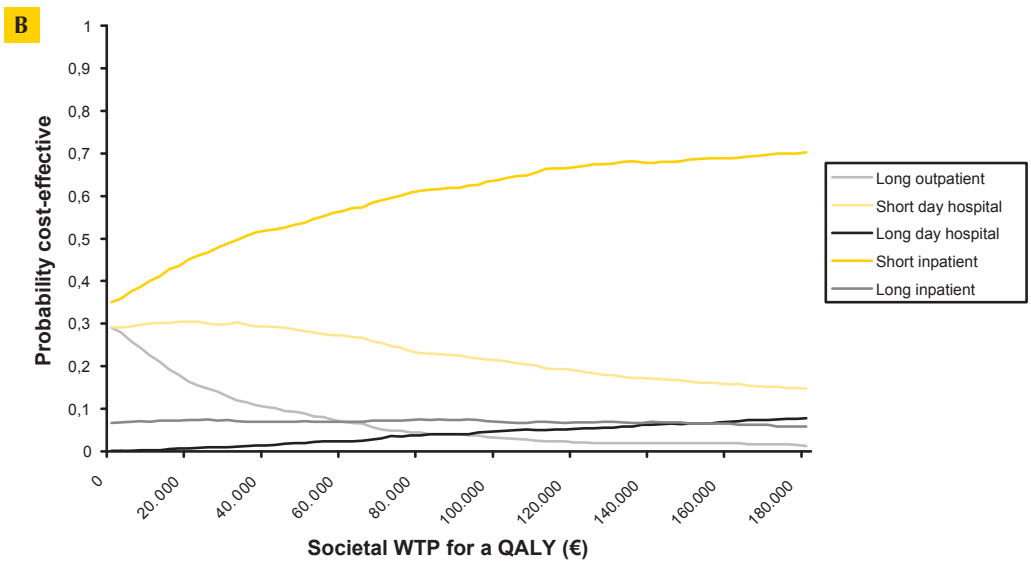
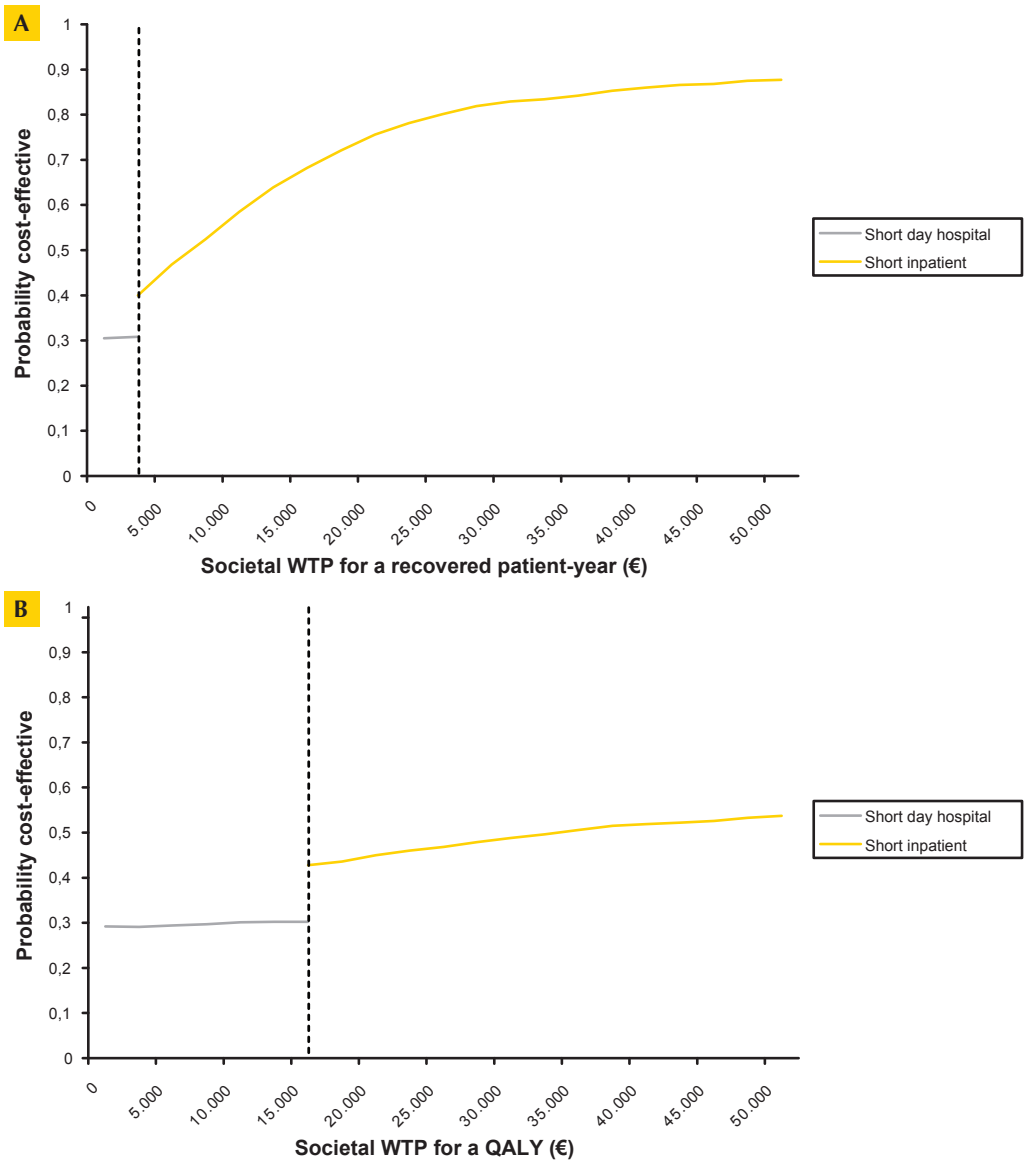


Figure 4.3 Cost-effectiveness acceptability frontiers (CEAF) showing the optimal dosage for each value of the societal WTP. A, CEAF for recovered patient-year. B, CEAF for QALY.



Footnote: The switch points, at which there is a change in the optimal option from short-term day hospital psychotherapy to short-term inpatient psychotherapy, were located at a threshold value of €2,637 per recovered patient-year and €16,570 per QALY.

Cost-effectiveness analysis from the payer perspective

The CEAF of cost per recovered patient-year and cost per QALY from the payer perspective show the same pattern of results as from the societal perspective, with short-term day hospital psychotherapy and short-term inpatient psychotherapy being the optimal treatments. However, the switch points were located at higher threshold values: €9,874 per recovered patient-year, and €66,302 per QALY (**Table 4.4**).

Discussion

Using decision-analytic modeling, we estimated the cost-effectiveness of five dosages of psychotherapy for cluster C PD over a five-year time horizon from both the societal and payer perspective. To our knowledge, this is the first economic evaluation focusing on various dosages of psychotherapy for this particular patient population. It is important to note that current clinical guidelines are confined to borderline PD, except for the Dutch multidisciplinary clinical guideline which spans the broad spectrum of PD.[6] However, all available guidelines are exclusively based on effectiveness data. This study therefore has the potential to contribute significantly to the knowledge base guiding rational decision making with respect to clinical practices and health care resource allocation.

This economic evaluation yields two cost-effective treatment options for cluster C PD. Our findings indicate that if societal WTP does not exceed €2,637 per recovered patient-year or €16,570 per QALY, short-term day hospital psychotherapy provides the highest expected net benefit and can be considered the preferred option. Above these values, short-term inpatient psychotherapy is the optimal choice. Reasonably we can assume that society is willing to spend more than €2,637 per recovered patient-year and thus, in terms of cost per recovered patient-year, short-term inpatient psychotherapy is the optimal choice. Our results in terms of cost per QALY can be interpreted according to recommendations by the Dutch council for Public Health and Health care.[30] For acutely life-threatening illnesses (with a maximum burden of disease), an explicit maximum of €80,000 per QALY was recommended. For less life-threatening illnesses that only affect quality of life, the council recommends a proportional lower acceptable threshold. Cluster C PD are associated with a severe impairment in quality of life.[4] The observed burden of 0.47 (i.e., mean EQ-5D index value of 0.53; range, 0.52 to 0.54) indicates that treatments may cost up to €37,600 per QALY to be acceptable. Based on this threshold value, short-term inpatient psychotherapy can be identified as the most cost-effective and thus optimal option as it provides the greatest benefit below the threshold.

Differences in health effects among strategies were more pronounced when outcomes were expressed in terms of recovered patient-years than in terms of QALYs. While this phenomenon has been reported previously by a cost-effectiveness analysis comparing two psychotherapies for borderline PD,[31] it seems surprising because two independent studies reported a Pearson correlation coefficient of -0.49 between the EQ-5D and recovery measures, indicating reasonable convergence.[32,33] Our results suggest that despite the sensitivity of the EQ-5D in distinguishing quality of life associated with particular health states, QALYs are nonetheless less adequate measures for discriminating levels of change between the different dosages of psychotherapy. Despite the observed divergence, however, the cost-effectiveness results for the two effect mea-

sures were qualitatively consistent, thereby supporting the robustness of the findings.

Interestingly, it appears that a dosage that initially seems expensive (i.e., short-term inpatient psychotherapy; treatment costs €25,933) turns out to be the most cost-effective option over time when costs due to other health care utilization and productivity losses are accounted for. In contrary, the dosage that initially seems the cheapest (i.e., long-term outpatient psychotherapy; treatment costs €10,005) is unmasked as a less cost-effective treatment. These findings demonstrate the added value of cost-effectiveness analysis from a broader perspective than just the treatment costs.

Several clinical implications can be derived from our analyses. From a health-economic perspective, short-term inpatient psychotherapy and short-term day hospital psychotherapy should be considered the options of first choice for patients with cluster C PD, based on accepted willingness to pay thresholds. Interestingly, this conclusion is consistent with several efficacy and effectiveness studies.[7] Note however, that this study is intended to inform recommendations from the public health (i.e., population) perspective and is not inherently designed to inform decision making at the individual level. Although we used primary patient-level data from a clinical study, we used those data to inform population averages (and plausible ranges) for our parameters. As a result, we were limited in our ability to examine individual-level heterogeneity such that there will undoubtedly be some patients, for example, for whom another treatment dosage may be the best option. Also, we find it important to emphasize that cost-effectiveness is only one aspect of medical decision making; other important factors that were not considered in our model include (1) strong patient preference for another option, or (2) contraindications for short- term day hospital or inpatient treatment. The latter may be the case in those patients who lack the psychological strength required to profit from such treatments that are usually characterized by a rather confrontational or expressive therapeutic milieu.[7] It is important to note, however, that our results identify long-term outpatient psychotherapy, long-term day hospital psychotherapy, and long-term inpatient psychotherapy as sub-optimal treatment options for this patient group. Future research should investigate patient-treatment matching hypotheses in this respect. Moreover, although the patient group under study is homogeneous in the sense that they all have cluster C personality disorders, the potential for the resulting cost-effectiveness to vary across different subgroups should be examined.

The major strength of this study was the collective use of the state of the art technology and patient-level primary data to estimate the cost-effectiveness of health care interventions. Decision-analytic modeling provides a framework for informed decision making under conditions of uncertainty. Furthermore, the availability of primary data from such a large patient trial provided a unique opportunity to inform the parameters of our model, as most modeling studies are based on secondary data.

Our analysis has a number of limitations. First, the model is developed using data from a treatment-seeking patient population, and in particular for those who seek specialized psychotherapy for personality problems. Therefore, the applicability of the results to non-treatment seekers, forensic care, or patients who admit with a primary Axis I diagnosis, is limited. Second, this study compares only dosage, whereas the included treatments may also differ in terms of other characteristics such as theoretical orientation and therapeutic techniques. This limitation is somewhat mitigated by studies showing that theoretical orientation as a treatment parameter might only account for minor differences in effects – if any,[34,35] and is not likely to be associated with costs. Finally, the data source for our model was a nonrandomized clinical trial that might

be limited because patients were not randomized over treatment conditions. However, this apparent drawback might be considered an advantage within the context of economic evaluations, because nonrandomized studies are likely to be more representative and thus externally valid with respect to costs and effects.[11,12] Moreover, randomization between existing treatment options is no longer feasible, because once information about a therapy's clinical effectiveness is available, patients may not be willing to participate in experiments simply to evaluate its value for the cost. Exactly because of this reason, the same research group recently failed to conduct a randomized clinical trial comparing inpatient and outpatient psychotherapy for cluster C PD. To overcome the problem of selection bias, we controlled for initial differences in patient characteristics with the propensity score method.[26]

It can be concluded from our model-based analysis that short-term day hospital psychotherapy and short-term inpatient psychotherapy are the optimal treatment dosages for cluster C PD in terms of cost per recovered patient-year and cost per QALY, while the ultimate choice depends on what cost-effectiveness threshold is acceptable. It is important to note that the decision for the optimal choice is surrounded by uncertainty, and that there is a possibility of making a wrong decision on a patient level. In order to reduce the uncertainty associated with that decision, future work should include a so-called value of information analysis which addresses whether or not it is cost-effective to undertake additional research regarding one or more uncertain parameters in the decision model.

Appendix A. Mean six-month probabilities of transitioning from one state to another in each time period, after propensity score adjustment

To →	First six month probabilitiesa				
From ↓	Recovered	Improved	Unchanged	Relapsed/det	Death
Long outpatient	0,23	0,11	0,48	0,18	—
Short day hospital	0,21	0,07	0,60	0,12	—
Long day hospital	0,42	0,13	0,23	0,22	—
Short inpatient	0,69	0,07	0,20	0,04	—
Long inpatient	0,43	0,11	0,32	0,14	—

a In the first six months patients enter the model. The percentage of patients in each of the five health states is displayed. We assumed no probability of death.

From recovered to recovered

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,68	0,70	0,68	0,83	0,76
Shortday	0,84	0,76	0,87	0,92	0,90
Longday	0,77	0,74	0,88	0,86	0,87
Shortin	0,83	0,74	0,85	0,84	0,84
Longin	0,79	0,78	0,85	0,89	0,87

From recovered to improved

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,06	0,07	0,08	0,08	0,08
Shortday	0,05	0,08	0,03	0,03	0,03
Longday	0,12	0,10	0,04	0,02	0,03
Shortin	0,12	0,15	0,07	0,05	0,06
Longin	0,10	0,05	0,05	0,07	0,06

From recovered to unchanged

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,20	0,17	0,18	0,04	0,11
Shortday	0,05	0,11	0,06	0,03	0,05
Longday	0,08	0,13	0,05	0,09	0,07
Shortin	0,02	0,09	0,05	0,08	0,06
Longin	0,09	0,14	0,07	0,02	0,05

From recovered to relapsed/deteriorated

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,06	0,07	0,06	0,04	0,05
Shortday	0,05	0,05	0,03	0,03	0,03
Longday	0,03	0,03	0,03	0,02	0,03
Shortin	0,02	0,03	0,03	0,03	0,03
Longin	0,02	0,03	0,03	0,02	0,02

From unchanged to unchanged

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,88	0,82	0,69	0,80	0,74
Shortday	0,79	0,70	0,80	0,67	0,73
Longday	0,80	0,68	0,68	0,67	0,67
Shortin	0,79	0,65	0,52	0,72	0,62
Longin	0,72	0,77	0,75	0,82	0,79

From unchanged to recovered

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,03	0,06	0,16	0,07	0,11
Shortday	0,10	0,18	0,09	0,13	0,11
Longday	0,05	0,17	0,20	0,20	0,20
Shortin	0,07	0,13	0,27	0,09	0,18
Longin	0,16	0,09	0,12	0,09	0,10

From unchanged to improved

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,06	0,07	0,11	0,03	0,07
Shortday	0,07	0,07	0,05	0,11	0,08
Longday	0,10	0,08	0,09	0,09	0,09
Shortin	0,07	0,13	0,10	0,10	0,10
Longin	0,09	0,11	0,08	0,06	0,07

From unchanged to relapsed/deteriorated

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,03	0,05	0,05	0,10	0,08
Shortday	0,04	0,05	0,06	0,10	0,08
Longday	0,05	0,07	0,04	0,05	0,04
Shortin	0,07	0,10	0,12	0,09	0,10
Longin	0,03	0,03	0,06	0,03	0,04

From improved to improved

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,70	0,63	0,52	0,59	0,55
Shortday	0,48	0,67	0,54	0,67	0,60
Longday	0,57	0,52	0,63	0,57	0,60
Shortin	0,39	0,35	0,53	0,49	0,51
Longin	0,60	0,67	0,66	0,42	0,54

From relapsed/deteriorated to relapsed/deteriorated

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,45	0,25	0,42	0,56	0,49
Shortday	0,44	0,44	0,45	0,24	0,34
Longday	0,56	0,48	0,35	0,20	0,28
Shortin	0,50	0,36	0,39	0,54	0,47
Longin	0,54	0,25	0,50	0,34	0,42

From improved to recovered

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,10	0,18	0,16	0,20	0,18
Shortday	0,29	0,14	0,23	0,11	0,17
Longday	0,21	0,31	0,20	0,12	0,16
Shortin	0,27	0,45	0,25	0,15	0,20
Longin	0,07	0,16	0,12	0,25	0,19

From relapsed/deteriorated to recovered

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,07	0,25	0,17	0,14	0,16
Shortday	0,08	0,18	0,23	0,10	0,16
Longday	0,05	0,10	0,16	0,17	0,17
Shortin	0,17	0,17	0,25	0,13	0,19
Longin	0,06	0,25	0,17	0,11	0,14

From improved to unchanged

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,10	0,09	0,24	0,14	0,19
Shortday	0,11	0,09	0,16	0,11	0,14
Longday	0,15	0,10	0,10	0,24	0,17
Shortin	0,21	0,10	0,14	0,27	0,21
Longin	0,26	0,10	0,16	0,28	0,22

From relapsed/deteriorated to improved

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,07	0,25	0,17	0,14	0,16
Shortday	0,08	0,11	0,13	0,10	0,11
Longday	0,05	0,14	0,13	0,17	0,15
Shortin	0,17	0,18	0,17	0,13	0,15
Longin	0,06	0,25	0,13	0,11	0,12

From improved to relapsed/deteriorated

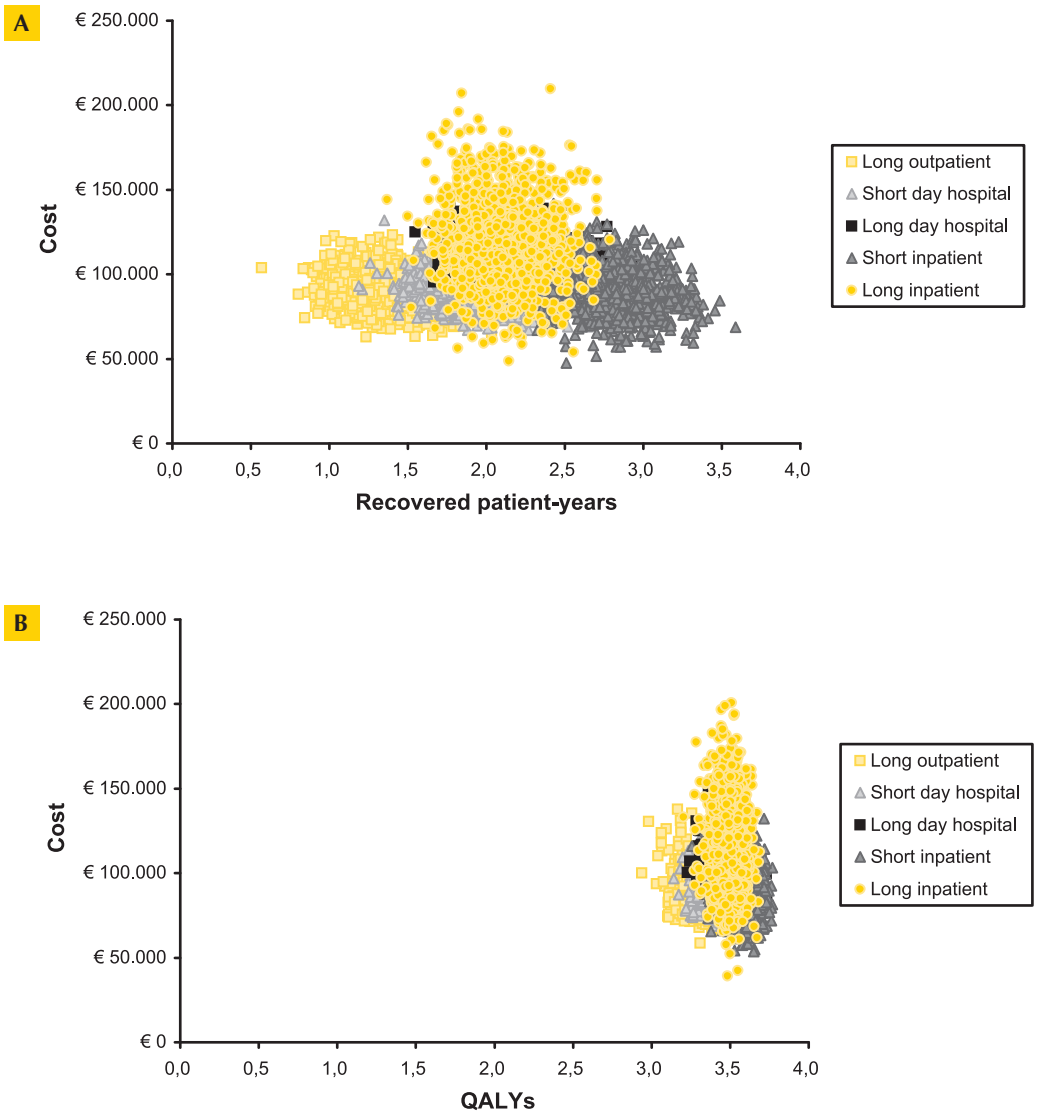
	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,10	0,09	0,08	0,07	0,08
Shortday	0,11	0,10	0,06	0,11	0,09
Longday	0,08	0,07	0,07	0,07	0,07
Shortin	0,13	0,10	0,07	0,08	0,08
Longin	0,07	0,06	0,05	0,05	0,05

From relapsed/deteriorated to unchanged

	6-12m	12-24m	24-36m	36-42m	42-60m
Longout	0,40	0,25	0,24	0,16	0,20
Shortday	0,40	0,27	0,20	0,56	0,38
Longday	0,33	0,29	0,36	0,46	0,41
Shortin	0,17	0,30	0,19	0,21	0,20
Longin	0,34	0,25	0,21	0,44	0,32

Footnote: In the reported transition probabilities the risk of death was not taken into account. In our model however we used a probability of death obtained from standard life tables which varies according to time in model (i.e., age-specific background mortality). Moreover, we assumed patients in the improved, unchanged and relapsed or deteriorated health states faced an elevated risk of death of 0.00127 due to suicide.

Appendix B. Scatter plots showing the costs and health outcomes of the treatment strategies from 1000 Monte Carlo simulations. A, for recovered patient-years. B, for QALYs.



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Cost-Effectiveness of Psychotherapy for Cluster B Personality Disorders

Chapter 5

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Abstract

Background

Recommendations of current clinical guidelines are informed by limited economic evidence.

Aims

A formal economic evaluation of three modalities of psychotherapy for patients with cluster B personality disorders.

Method

A probabilistic decision-analytic model to assess the cost-effectiveness of outpatient, day hospital, and inpatient psychotherapy over 5 years in terms of cost per recovered patient-year and cost per quality-adjusted life year (QALY). Analyses were conducted from both societal and payer perspectives.

Results

From the societal perspective, the most cost-effective choice switched from outpatient to day hospital psychotherapy at a threshold of €12,274 per recovered patient-year; and from day hospital to inpatient psychotherapy at €113,298. In terms of cost per QALY, the optimal strategy changed at €56,325 and €286,493 per QALY, respectively. From the payer perspective, the switch points were at €9,895 and €155,797 per recovered patient-year, and €43,427 and €561,188 per QALY.

Conclusions

Outpatient psychotherapy and day hospital psychotherapy are the optimal treatments for patients with cluster B personality disorders in terms of cost per recovered patient-year and cost per QALY.

Introduction

Cluster B personality disorders (PD), including borderline, antisocial, histrionic, and narcissistic PD, are among the most prevalent mental disorders in the general population[1,2] and mental healthcare settings.[3,4] Moreover, these disorders are associated with high societal costs and a low quality of life.[5,6] Although different in many respects, a common feature of cluster B PD is a rather dramatic and impulsive manifestation that is considered more persistent and resistant to change than cluster C PD (i.e., avoidant, dependent, and obsessive-compulsive PD) but less so than cluster A PD (i.e., paranoid, schizoid, and schizotypal PD). Currently, several treatments with demonstrated efficacy for borderline PD are being adapted and tested for antisocial PD, suggesting a partially common nature to these disorders.[7] Additionally, contemporary classification models of PD increasingly focus on dimensions rather than categories, and cluster B PD seem to have similarly high scores on dimensions of behavioral and emotional disinhibition, and antagonism.[8] This paradigm shift makes it clinically relevant to include the full range of cluster B PD in analyses rather than focus solely on the more common borderline PD.

A multidisciplinary clinical guideline in the Netherlands recently identified various modalities of psychotherapy, including outpatient, day hospital, and inpatient psychotherapy, to be preferential for cluster B PD[9], consistent with two other clinical guidelines that focused on borderline PD.[10,11] While based on strong evidence of efficacy,[12] the economic impact of these recommendations has not yet been explored, and few cost-effectiveness analyses of PD interventions exist that can guide decision making with respect to clinical practices and health care resource allocation. Recently, the Study on Cost-Effectiveness of Personality disorder Treatment (SCEPTRE) was conducted with the purpose of providing data for economic evaluations of various psychotherapeutic treatments for PD. Used in a decision-analytic framework, the data on health benefits and resource use from this study can be synthesized to evaluate the relative performance of health interventions under conditions of uncertainty and imperfect data.[13] The objective of this study was to assess the cost-effectiveness of three modalities of psychotherapy in treating cluster B PD (i.e., outpatient psychotherapy, day hospital psychotherapy, and inpatient psychotherapy) and to inform decision makers about the value of these treatment options. We incorporated clinical and economic patient-level data from the SCEPTRE trial in a simulation model to compare the strategies over a five-year time horizon in terms of costs per recovered patient-year and costs per quality-adjusted life year (QALY).

Methods

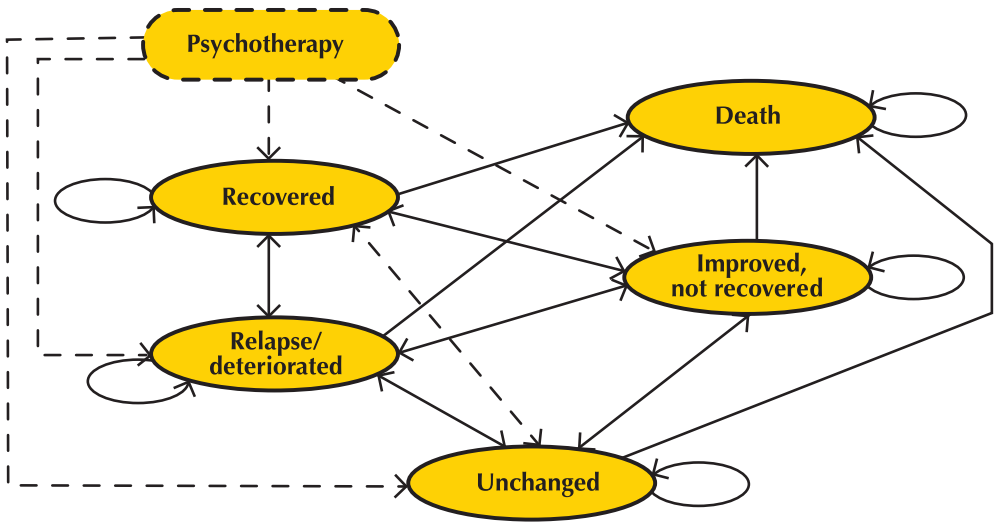
Model

We used a previously-developed Markov cohort model[13,14] to simulate the transition of a cohort of patients with cluster B PD through mutually-exclusive and collectively exhaustive health states over time, based on data from the SCEPTRE trial. The model is then used to estimate the impact of different interventions on the patient population. The underlying clinical process driving the current model and by which the health states are defined is 'clinically significant change', based on a statistical approach to defining meaningful change in psychotherapy research.[15] To calculate the cut off points and the reliable change index required for this approach, norm scores based on the Symptom Checklist-90 Revised (SCL-90-R) were used as treatment outcome measures for both the functional and the dysfunctional population.[16] Patients are classified into one of four health states: (1) recovered (if the magnitude of change is statistically reliable and

the patient ends up within normal limits on the variable of interest), (2) improved (if the patient shows statistically reliable change but ends therapy still somewhat dysfunctional), (3) unchanged (if the magnitude of change is not statistically reliable, the method cannot determine whether or not the change is clinically significant), and (4) relapsed or deteriorated (if a statistically reliable change is in the opposite direction to that indicative of improvement). At anytime, patients can also die from suicide or age-specific background mortality. The structure of the Markov model is shown in **Figure 5.1**.

Four types of parameters were used in the model: (1) transition probabilities, which govern the movement between the five states at each cycle, (2) treatment costs of the three modalities of psychotherapy, (3) costs of health care utilization and productivity losses incurred by patients in each state, and (4) health state utilities, which reflect the health-related quality of life experienced by patients in each state. These data were obtained from a single patient-level data source (i.e., the SCEPTRE trial), a nonrandomized clinical trial. Strengths and limitations of the study design have been discussed elsewhere.[17,18] To overcome the problem of selection bias, we controlled for initial differences in patient characteristics with the propensity score method (see below). The results are based on intention-to-treat analyses.

Figure 5.1 State transition diagram of the Markov model for psychotherapy



Transitions between health states in the model was assumed to occur at a constant interval of every six months, corresponding to multiple changes in pathology, symptoms, treatment decisions, or costs for patients with PD.

To be consistent with many other trial-based economic evaluations in the literature, we chose a five-year time horizon, which is two years beyond the duration of the clinical trial.

With respect to the transition probabilities, we extrapolated for the last two years of the analysis and considered several methods of extrapolation. Based on the trends observed during the study, we elected to average the last two observations (i.e., years 2 and 3) from the trial and hold those values constant in years 4 and 5 of the analysis. For other model inputs, data collection did not stop at three years; indeed, we relied on questionnaires that were administered in the fourth year to estimate the costs and utilities associated with different health states and kept these values constant for the fifth year. We reported results as costs per recovered patient-year and costs per quality-adjusted life year (QALY) over the five years using the model; costs and QALYs were discounted at an annual rate of 4.0% and 1.5% respectively, consistent with guidelines for economic evaluations in the Netherlands.[19] In a sensitivity analysis, we studied the impact of applying a 3% discount rate for both costs and health outcomes as recommended by UK and US economic guidelines. The base case analysis was conducted from the societal perspective, and a secondary analysis from the payer perspective.

Table 5.1 Demographic and clinical characteristics of 241 study participants

Modality of psychotherapy	Outpatient	Day hospital	Inpatient
	(n=57)	(n=99)	(n=85)
Age, mean (SD), y	35.4 (8.7)	31.4 (8.2)	28.9 (7.2)
Sex %			
Female	64.9	76.8	70.6
Comorbidity Axis II %			
pure cluster B (no comorbid cluster A/C)	33.3	37.4	48.2
cluster B and cluster A	8.8	0	3.5
cluster B and cluster C	49.1	45.5	40.0
cluster B and both cluster A and C	8.8	17.2	8.2
Personality disorder %			
borderline	71.9	80.8	80.0
narcissistic	29.8	22.2	18.8
histrionic	19.3	9.1	14.1
antisocial	8.8	5.1	3.5

Recruitment and assignment

Patients were recruited from a consecutive series of admissions to six mental health care institutes in the Netherlands offering specialized psychotherapy for adult patients with PD. Diagnoses were based on the Dutch version[20] of the Structured Interview for DSM-IV Personality (SIDP-IV).[21] For this particular analysis, inclusion criteria were a diagnosis of cluster B PD, age 18 to 70 years, assignment to a specified dosage of psychotherapeutic treatment for PD, and Dutch literacy. Exclusion criteria were psychotic disorders (e.g., schizophrenia), organic cerebral impairment, and mental retardation. Comorbid Axis I and Axis II disorders were allowed.

From March 2003 to March 2006, 1379 individuals completed the intake procedure and were selected for various treatment options. Of those, 241 patients were eligible, provided informed consent, and entered the study (**Table 5.1**). Patients were assigned to one of three treat-

ment groups, based on a comprehensive assessment battery combined with the expert opinion of clinicians: outpatient, day hospital, and inpatient psychotherapy. In the outpatient strategy, patients are offered up to two sessions per week. In the day hospital strategy, patients are offered psychotherapy combined with sociotherapy and/or non-verbal therapies for 1-5 days per week. The inpatient strategy offers the same, but patients reside in the treatment centers 5-7 days per week. Mean (SD) duration of treatment for these three strategies was 15.1 (7.1), 10.4 (4.7), and 9.3 (2.9) months, respectively.

Input data

Transition probabilities – The proportion of patients in each of the health states was determined at 6, 12, 18, 24, 30, and 36 months after baseline from the SCEPTRE trial. Based on the difference between the frequency distributions over time, the probabilities of transitioning from one state to another in each six-month time period were calculated. Transition probabilities among the recovered, improved, unchanged, and relapsed or deteriorated health states are available upon request.

Costs – Costs were estimated from both societal and payer perspectives. The calculations from the societal perspective included direct medical costs (i.e., primary treatment costs and costs of health care utilization post-discharge) and direct non-medical costs (i.e., lost productivity due to time spent in treatment), as well as indirect costs (i.e., future lost productivity due to disease), while the payer perspective included only direct medical costs. Mean primary treatment costs for the three strategies were calculated by multiplying the resource quantities with the 2007 unit costs or prices of the corresponding treatment options. We obtained data from the hospital finance departments on staff salaries, equipment, buildings and departmental overheads, and used a micro-costing approach to derive the cost of a treatment session and an inpatient day. The resource quantities were collected from the hospital data systems. Costs due to productivity loss because of patients' time in treatment were also estimated and included in the analysis from the societal perspective. For patients with paid employment at enrollment, mean costs were calculated by multiplying the actual days (inpatient psychotherapy, day hospital psychotherapy) and hours (outpatient psychotherapy) spent in treatment by the net income of the patient per day and per hour, respectively. The mean (SE) treatment costs were €7,445 (511) for outpatient psychotherapy, €23,279 (1,738) for day hospital psychotherapy, and €35,218 (1,354) for inpatient psychotherapy.

Post-discharge costs due to health care utilization and productivity losses, likely to be substantial, were also included. The Trimbos and Institute for Medical Technology Assessment (iMTA) Questionnaire on Costs Associated with Psychiatric Illness (TiC-P) was used to collect data on direct medical and indirect costs.[22] For direct medical costs, the total number of medical visits (e.g. outpatient visits, hospital lengths of stay, use of medication) was multiplied by the 2003 unit prices of the corresponding health care services.[23,24] The reference unit prices of health care services for 2003 were adjusted to prices in 2007 using the consumer price index.[25] The mean direct medical costs over the recall period of the TiC-P (i.e., four weeks) were multiplied by 6.5 to calculate the six-month costs to correspond to the model cycle length. For indirect costs, we obtained data on absence from work, reduced efficiency at work, and difficulties with job performance from the TiC-P short form of the Health and Labor Questionnaire.[26] The days

of short-term absence from work and actual hours missed at work because of health-related problems were multiplied by the net income of the patient per day and per hour, respectively. The number of lost working days per patient was calculated, taking into account the number of days and hours of paid employment of the patient per week. To value long-term absence from work, we applied the friction-cost method, which takes into account the fact that a formerly unemployed person may replace a person who becomes disabled.[27] The period needed to replace a worker (the so-called friction period) is estimated to be five months; we therefore assumed the maximum indirect costs to society were limited to productivity losses during a period of five months. The cost estimates from the societal perspective used in the analysis are summarized in **Table 5.2**. For each strategy, the model calculates the expected cost by taking a weighted average of the costs of each health state and the proportion of the cohort in each health state at each six-month period; the total expected cost of the strategy is then calculated by summing over the five year time horizon.

Table 5.2 Model parameters: Mean health state costs and utilities over time from the societal perspective

Health states		Recovered	Improved [c]	Unchanged	Relapsed or det.
Health state costs [a], mean (SE)					
years	1 to 2	€ 6,637 (3,064)	€ 9,639 (4,848)	€ 10,846 (3,763)	€ 24,481 (13,204)
	3	€ 2,472 (458)	€ 3,899 (1,013)	€ 5,705 (1,533)	€ 5,554 (2,312)
	4 to 5	€ 2,188 (491)	€ 11,395 (8,215)[d]	€ 4,751 (1,297)	€ 5,767 (2,830)
Health utilities [b], mean (SE)					
years	1	0.78 (0.03)	0.64 (0.11)	0.67 (0.06)	0.39 (0.10)
	2	0.82 (0.02)	0.65 (0.03)	0.59 (0.03)	0.47 (0.07)
	3	0.83 (0.02)	0.58 (0.05)	0.60 (0.04)	0.45 (0.18)
	4 to 5	0.87 (0.02)	0.67 (0.04)	0.69 (0.03)	0.34 (0.15)

a Mean cost estimates of a half year spent in each of the model health states. Estimates include post-discharge costs due to health care utilization and productivity losses. As costs may vary according to time in model we calculated different cost estimates for the first two years, third, and last two years in the model.

b Mean quality of life utilities of a year spent in each of the model health states. In the model the reported utility weights were divided by two to fit the half-yearly cycle. As quality of life may vary according to time in model we calculated different utility weights for yearly time intervals until year three. For the last two years in the model a constant utility weight was used.

c The improved state includes both patients who start relatively well and improve, and who start sicker and improve, which on average will equal the unchanged scores.

d Several patients induced very high costs due to costly services, such as long-term admissions into inpatient treatment settings, and long-term absence from work.

Health utilities – To reflect the diminished quality of life of patients with PD, health utility weights were assigned to each health state, based on the EuroQol EQ-5D which records quality of life in five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.[28] Each dimension is divided into three response levels: no problems, some or moderate problems,

and extreme problems or complete inability. A total of 243 different possible health states are each weighted to derive a single index score between –0.33 (worst imaginable health state) and 1.00 (best imaginable health state). The Dutch norm scores were used for calculating the mean EQ-5D index values.[29] The mean quality of life utilities of a year spent in each of the model health states for each cycle are summarized in **Table 5.2**. The expected number of QALYs for each strategy was estimated by weighing the duration of time in a particular health state by the utility of that health state and then summing over all health states in each cycle. The expected number of QALYs per patient over five years was calculated by summing over all cycles.

Mortality rates – Patients in the recovered health state were assumed to face a risk of death equivalent to that observed in the general population. These age- and sex-specific mortality rates were obtained from standard life tables.[30] Moreover, we assumed patients in the improved, unchanged and relapsed or deteriorated health states faced an elevated risk of death due to suicide, based on the SCEPTRE data.

Propensity score method

To overcome the problem of selection bias, we controlled for initial differences in patient characteristics with the multiple propensity score method.[31] The estimated propensity score is defined as the conditional probability of assignment to a particular treatment, given a set of observed pre-treatment characteristics. Details of the method and the variables used to estimate the propensity scores are described elsewhere.[32] Multinomial regression analyses were conducted to adjust the transition probabilities for the multiple propensity scores.

Analysis

In order to reflect uncertainty in our parameter values, we conducted a probabilistic analysis in which distributions were assigned to the input parameters of the model (i.e., gamma distributions for costs, beta distributions for utilities, and Dirichlet distributions for probability parameters).[13] Multiple simulations were conducted in which a single value for each parameter was randomly sampled from the corresponding distribution, creating a unique parameter set. One thousand parameter sets were sampled and used in the model to calculate the expected costs, expected recovery rate, and QALY for each strategy.

The mean values of costs, recovered patient-years, and QALYs across all 1000 simulations were used to calculate incremental cost-effectiveness ratios (ICER) associated with each strategy, defined as the additional cost divided by the additional health benefit associated with one strategy as compared with the next-less-costly strategy. The most cost-effective strategy was then identified by comparing the ICERs of different strategies against various threshold values, which reflect the decision maker's willingness-to-pay (WTP) for an additional unit of effect. Strategies below a specific WTP value generally represent good value for money; the "most cost-effective" strategy is the strategy with the highest ICER below the WTP threshold, representing the option that yields the highest level of benefit for an acceptable cost.

In order to report on the impact of the uncertainty in the parameter values, cost-effectiveness acceptability curves (CEAC) were created to indicate the probability of each option being cost-effective conditional on the decision maker's WTP for a recovered patient-year or QALY.[33] Finally, the cost-effectiveness acceptability frontier (CEAF) was plotted to portray each CEAC over the range of threshold values for which each option is estimated to be the most cost-

effective, as well as the threshold ICER at which there are changes in the optimal modality (i.e., "switch points").[34]

Results

Five-year costs and health outcomes

The mean five-year costs and health outcomes from the societal perspective are presented in **Table 5.3**. The table shows that the mean costs are substantially lower for outpatient psychotherapy, suggesting that the higher treatment costs of the day hospital and inpatient modalities are not offset by savings elsewhere, such as reductions in costs due to health care utilization and productivity losses. The rank ordering of strategies by effect is the same for both recovered patient-years and QALYs, indicating inpatient psychotherapy as the most effective option. With respect to the percentage of patients residing in the recovered health state at year five, day hospital psychotherapy is associated with the highest percent recovered. Outpatient psychotherapy appears to be consistently the least effective option.

Table 5.3 Discounted costs and health outcomes over five years from the societal perspective

Modality of psychotherapy	costs [a]	recovered patient-years [b]	costs [a]	QALYs [c]	% recovered [d]
Outpatient	€ 78,548	1.1449	€ 80,247	3.1080	24.7
Day hospital	€ 89,323	2.0227	€ 91,090	3.3005	48.6
Inpatient	€ 96,264	2.0840	€ 97,351	3.3223	36.1

a Values represent mean costs per patient, including treatment costs and costs involved with spending time in each of the model health states.

b Mean number of years spend in the recovered health state per patient.

c Mean number of QALYs gained per patient.

d Percentage of patients resided in the recovered health state at year five.

Cost-effectiveness analysis from the societal perspective

The cost-effectiveness ratios for each strategy, reported as cost per recovered patient-year and cost per QALY over a five-year time horizon, are displayed in **Table 5.4**. Outpatient psychotherapy yields the lowest costs and health benefits; day hospital psychotherapy shows higher costs and effects and was associated with an ICER of €12,274 per recovered patient-year and an ICER of €56,325 per QALY compared to outpatient psychotherapy. Inpatient psychotherapy yields the highest costs and health benefits and was associated with an ICER of €113,298 per recovered patient-year and an ICER of €286,493 per QALY compared to day hospital psychotherapy.

Table 5.4 Cost-effectiveness from the societal perspective over a five-year time horizon[a]

Modality of psychotherapy	Cost per recovered patient-year	Cost per QALY
Outpatient	-	-
Day hospital	€ 12,274	€ 56,325
Inpatient	€ 113,298	€ 286,493

a The values represent incremental cost-effectiveness ratios (ICER) i.e., the additional cost divided by the additional health benefit compared with the next-less-costly treatment, expressed as cost per recovered patient-year and cost per QALY. Note: because of rounding errors there may be some discrepancy between the results presented in this table and calculations when using the values from Table 3.

To display the impact of parameter uncertainty, we plotted the relationship between cost and health outcomes for each of the three competing psychotherapy modalities over 1000 simulations in the cost-effectiveness plane (**Figure 5.2**). When plotting costs against recovered patient-years (panel A), we found substantial uncertainty about both costs and effects for all treatment options. When using QALYs as the health measure (panel B), we found equal uncertainty about costs, whereas the uncertainty in effect was less substantial. The observed differences among the three treatment modalities relating to the effects were more pronounced in terms of recovered patient-years than QALYs.

Figure 5.2 Scatter plots showing the costs and health outcomes of the treatment strategies from 1000 Monte Carlo simulations. A, for recovered patient-years. B, for QALYs.

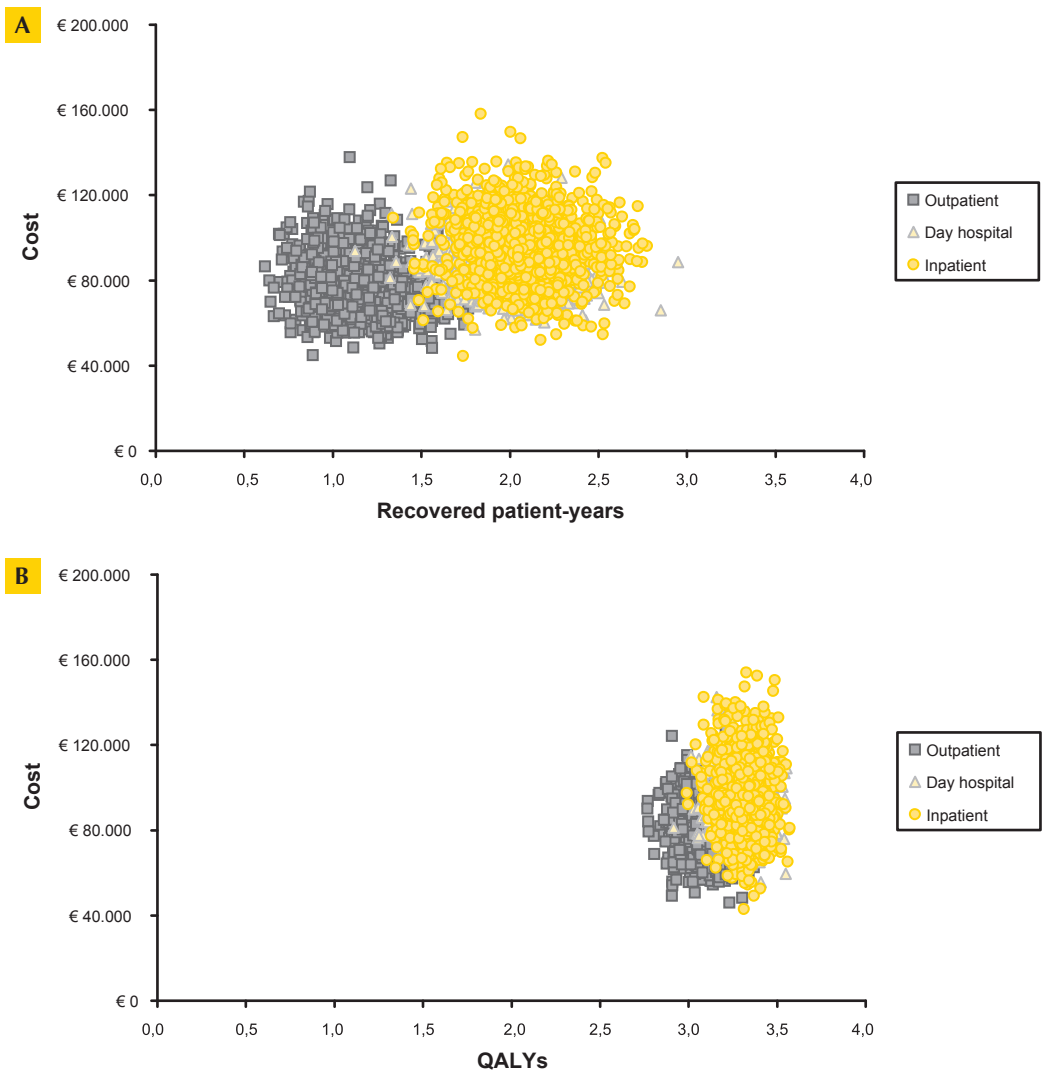


Figure 5.3 shows the cost-effectiveness acceptability curves (CEAC), which indicate the probability of each strategy being cost-effective at different values of the societal willingness-to-pay (WTP) for a unit of health benefit. In terms of cost per recovered patient-year, outpatient psychotherapy has the highest probability of being cost-effective for values of the societal WTP below €12,500. For values between €12,500 and €103,100 per recovered patient-year, day hospital psychotherapy is likely to be the most cost-effective. For values above €103,100 per recovered patient-year, inpatient psychotherapy has the highest probability of being cost-effective. In terms of costs per QALY, the same pattern of results can be observed, but the switch points were located at threshold values of €59,700 and €298,000, respectively. By definition, the CEAC crosses the Y-axis at the probability that the intervention under evaluation is cost-saving, as a WTP of zero implies that only cost determines cost-effectiveness (formula: WTP * Δeffects – Δcosts > 0).[35] According to the current analysis, outpatient psychotherapy has a probability of being cost-saving in approximately 84 percent of model simulations; in contrast, day hospital and inpatient psychotherapy have a negligible probability of being cost-saving.

While it is helpful to know the impact of uncertainty on results, the probability of a strategy being cost-effective is not sufficient to determine the optimal option. Decisions should be made on the basis of expected net benefit, regardless of the uncertainty associated with the decision.[33] To identify the optimal treatment option (i.e., the option with the highest expected net benefit for a given cost), the cost-effectiveness acceptability frontiers (CEAF) were plotted (**Figure 5.4**). The CEAF of cost per recovered patient-year shows the range of threshold values over which outpatient psychotherapy (€0 to €12,274), day hospital psychotherapy (€12,274 to € 113,298), and inpatient psychotherapy (above €113,298) have the highest expected net benefit and can be considered the optimal choice. The switch points, at which there is a change in the optimal option, correspond to the ICERs between outpatient and day hospital psychotherapy, and day hospital and inpatient psychotherapy. In terms of cost per QALY, the switch points were located at threshold values of €56,325 and €286,493, respectively. If society's WTP for a QALY is below the threshold value of €56,325 outpatient psychotherapy is the most cost-effective choice; above this value (and below €286,493), the optimal strategy would be day hospital psychotherapy. When we varied the discount rate to 3% per year for both costs and health outcomes, the optimal option changed from outpatient psychotherapy to day hospital psychotherapy and from day hospital psychotherapy to inpatient psychotherapy at threshold values of €12,120 and €132,866 per recovered patient-year, and €58,035 and €283,755 per QALY, respectively.

Cost-effectiveness analysis from the payer perspective

The CEAF of cost per recovered patient-year and cost per QALY from the payer perspective show the same pattern of results as from the societal perspective. However, the switch points were located at different threshold values: €9,895 and €155,797 per recovered patient-year, and €43,427 and €561,188 per QALY. When using a discount rate of 3% per year on outcomes, the switch points shifted marginally to threshold values of €9,495 and €204,278 per recovered patient-year, and €44,580 and €500,151 per QALY.

Figure 5.3 Cost-effectiveness acceptability curves (CEAC) showing the probability of each modality being cost-effective at different values of the societal WTP. A, CEAC for recovered patient-year. B, CEAC for QALY.

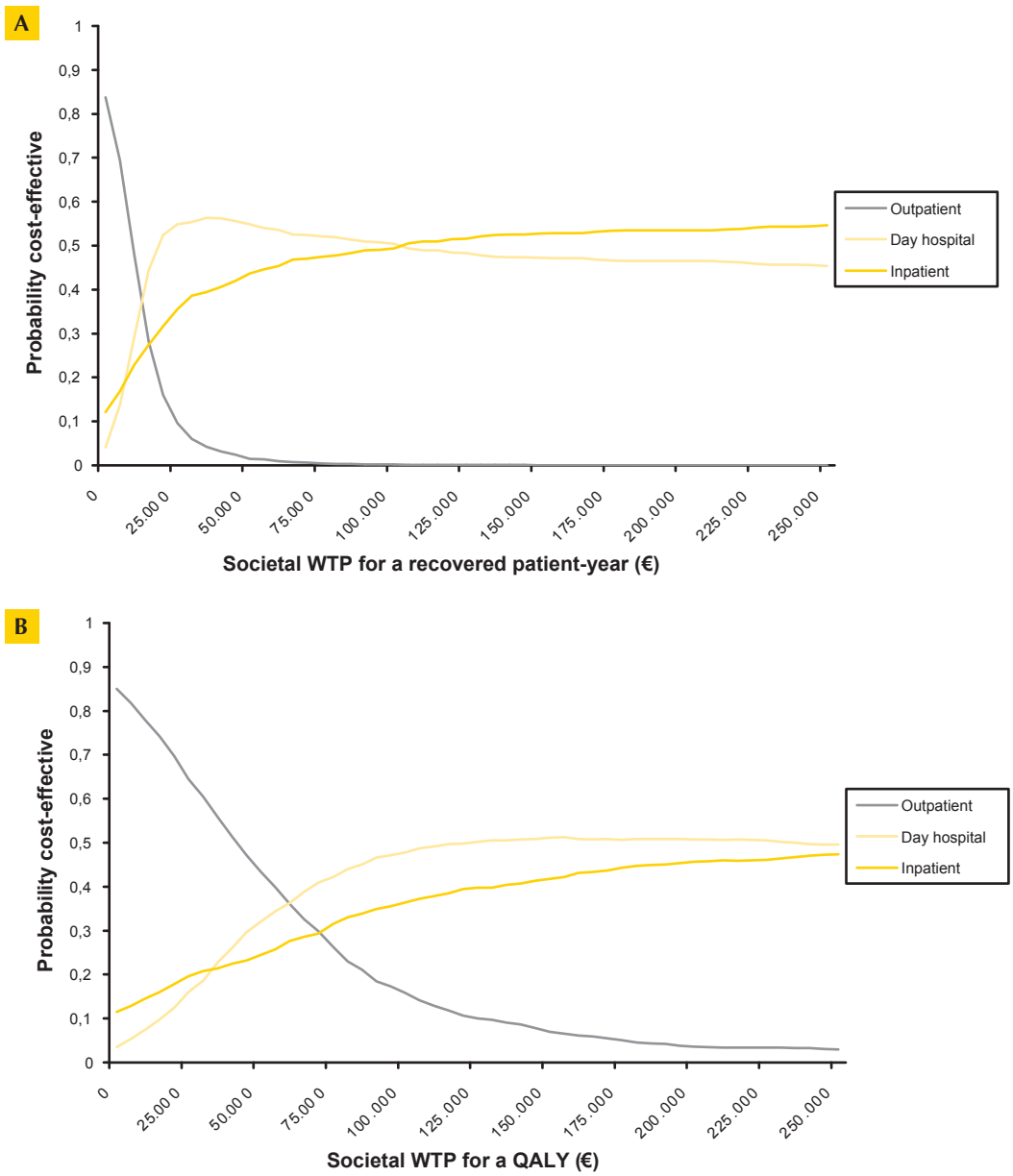
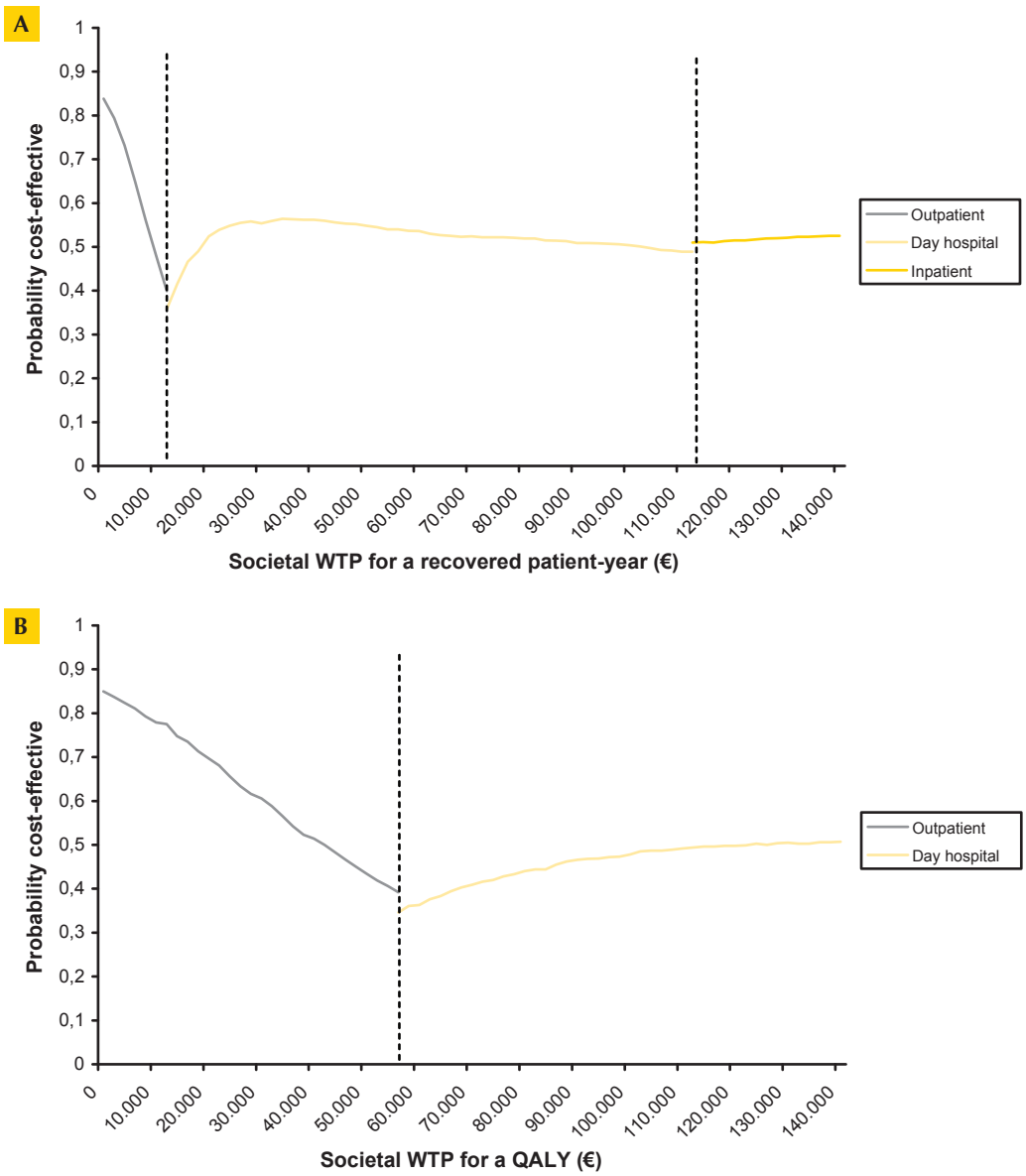


Figure 5.4 Cost-effectiveness acceptability frontiers (CEAF) showing the optimal modality for each value of the societal WTP. A, CEAF for recovered patient-year. B, CEAF for QALY.



Footnote: The switch points, at which there is a change in the optimal option from outpatient psychotherapy to day hospital psychotherapy and from day hospital psychotherapy to inpatient psychotherapy, were located at threshold values of €12,274 and €113,298 per recovered patient-year and €56,325 and €286,493 (not displayed in figure) per QALY.

Discussion

Using decision-analytic modeling, we estimated the cost-effectiveness of three modalities of psychotherapy for cluster B PD over a five-year time horizon from both societal and payer perspectives. To our knowledge, this is the first assessment of the cost-effectiveness of treatment modalities for this population based on a formal decision-analytic modeling approach. As recommendations of current clinical guidelines in the Netherlands have been informed by limited economic evidence, we believe this study has the potential to inform clinical decision making and health care resource allocations.

Our findings indicate that when the societal WTP does not exceed €12,274 per recovered patient-year, outpatient psychotherapy provides the highest expected net benefit. If society is willing to pay more than €12,274 per recovered patient-year, day hospital psychotherapy is the optimal choice. Notably, inpatient psychotherapy would not be considered the most cost-effective treatment modality unless the threshold value reached €113,298. Defining an acceptable threshold for a recovered patient-year is challenging, and without a common health metric, the cost-effectiveness ratios cannot be readily compared with interventions for other illnesses; for example, the costs of a cluster B PD recovered patient-year can only be compared to a depression recovered patient-year if they experience the same burden of disease. The use of QALYs as the health outcome allows for such a comparison across disease burdens, although there is no universally-accepted threshold value. Our results in terms of cost per QALY can be interpreted according to recommendations by the Dutch council for Public Health and Health care.[36] For acutely life-threatening illnesses (with a maximum burden of disease), an explicit maximum of €80,000 per QALY was recommended. For less life-threatening illnesses that only affect quality of life, the council recommends a proportional lower acceptable threshold. Cluster B PD are associated with a severe impairment in quality of life.[6] The observed burden of 0.49 (i.e., mean EQ-5D index value of 0.51; range, 0.50 to 0.52) indicates that treatments may cost up to €39,200 per QALY to be acceptable. Based on this threshold value, outpatient psychotherapy can be identified as the most cost-effective and thus optimal option as it provides the greatest benefit below the threshold.

The adoption decision for outpatient psychotherapy is robust over the discount rates applied, which could be expected because we only model outcomes over a five-year time horizon.

Our results suggest that the two cost-effectiveness measures with different health outcomes yield similar trends in results, with outpatient psychotherapy being the optimal intervention at low levels of the societal WTP, day hospital psychotherapy at higher levels, and inpatient psychotherapy at the highest levels. The switch points in terms of cost per QALY occurs at higher threshold values, which can be explained by the fact that the distinction between modalities regarding health benefits was more pronounced in terms of recovery rate than in terms of QALYs. Consequently, the relatively low costs of outpatient psychotherapy carries more weight in the calculations of cost per QALY than of cost per recovered patient-year and leads to more favorable results for outpatient psychotherapy. Previous studies have suggested that the EQ-5D may be insensitive in capturing changes in the quality of life of patients with borderline PD.[37,38] However, the health state utility weights calculated and used in the current analysis indicate that the EQ-5D, used to generate QALYs, can be considered sensitive to changes in patients with cluster B PD. For example, patients in the recovered health state show health utility weights (i.e., a quality of life) approaching the utility weight observed in the normal (nonclinical) population

(0.85); patients in the unchanged health state have a relatively stable utility weight compared to their value at enrollment (0.51); and patients in the relapsed or deteriorated health state were assigned much lower health utilities compared to enrollment. Despite the sensitivity of the EQ-5D in distinguishing quality of life associated with particular health states, QALYs are nonetheless less adequate measures for discriminating levels of change between the different modalities of psychotherapy.

The cost-effectiveness results for the two effect measures indicate that outpatient psychotherapy and day hospital psychotherapy are more cost-effective for cluster B PD than inpatient psychotherapy. Our findings are consistent with the scarce existing economic evidence identified by Brazier and colleagues in their systematic review evaluating the cost-effectiveness of psychological interventions for borderline PD.[38] Based on best available evidence, their review suggests that both outpatient and day hospital treatment (i.e., dialectical behavioral therapy and mentalization based therapy) are likely to be a cost-effective treatment modality for borderline PD.

Several clinical implications can be derived from our analyses. From a health-economic perspective, outpatient psychotherapy and day hospital psychotherapy should be considered the options of first choice for patients with cluster B PD, based on accepted WTP thresholds. Interestingly, this conclusion is consistent with several efficacy and effectiveness studies.[12] Note however, that this study attempts to inform recommendations from the public health (i.e., population) perspective and should be not used for individual decision making. Although we used primary patient-level data from a clinical study, we used those data to inform population averages (and plausible ranges) for our parameters. As a result, we were limited in our ability to examine individual-level heterogeneity such that there will undoubtedly be some patients for whom inpatient psychotherapy may be the best option. Also, we have to emphasize that cost-effectiveness is only one aspect of medical decision making, so in daily clinical practice other important factors that were not considered in our model must be considered, such as individual preferences, past history, insufficient or even pathogenic social support systems. Our study has identified inpatient psychotherapy as an effective but expensive option; future research should test patient-treatment matching hypotheses in this respect.

The major strength of this study was the collective use of the state of the art methodology and patient-level primary data to evaluate the cost-effectiveness of health care interventions. Decision-analytic modeling provides a framework for informed decision making under conditions of uncertainty. Specifically, it allows for exploration of the impact of uncertainty across multiple parameters simultaneously, and projection of results beyond the time horizon of the clinical trial. Furthermore, the availability of primary data from such a large patient trial provided a unique opportunity to inform the parameters of our model, as most modeling studies are based on secondary data. Data from future studies can be used to update the parameters of this existing probabilistic cost-effectiveness model.

Assumptions were made in this model-based analysis. To correspond to the model cycle length, the costs of health care utilization post-discharge were multiplied by 6.5 to estimate the half-yearly costs. The extrapolation of these costs is based on the assumption that the recall period of four weeks of the TiC-P is representative for half a year. This assumption was tested in the same population in a previously published study, indicating that on a population level there was no significant difference between the costs as measured with a recall period of a year compared to a recall period of four weeks.[5] We therefore believe that the costs calculated in

the present study are a reasonable estimation of the actual costs generated over the model cycle length of six months.

Our analysis has several limitations. First, the model is developed using data from a treatment-seeking patient population, and in particular for those who seek specialized psychotherapy for personality problems. Therefore, the applicability of the results to non-treatment seekers, forensic care, or patients who admit with a primary Axis I diagnosis, is limited. Second, despite the fact that this population is known to use criminal justice resources, these costs were not included in the analysis, which leads to an underestimation of the true societal costs. Third, this study compares only three modalities of psychotherapy, whereas the included treatments may also differ in terms of other characteristics such as theoretical orientation and therapeutic techniques. This limitation is somewhat mitigated by studies showing that theoretical orientation as a treatment parameter might only account for minor differences in effects – if any,[39,40] and is not likely to be associated with costs. This is however not true for duration as a treatment parameter; future research should therefore address optimal dosing in terms of treatment duration. Finally, our analyses were based on a clinical trial with a nonrandomized study design. That patients were not randomized over treatment conditions, however, is not a drawback but rather an advantage within the context of economic evaluations, because nonrandomized studies are likely to be more representative and thus externally valid with respect to costs and effects.[17,18] Moreover, randomization between existing treatment options is no longer feasible, because once information about a therapy's clinical effectiveness is available, patients may not be willing to participate in experiments simply to evaluate its value for the cost. Exactly because of this reason, the same research group recently failed to conduct a randomized clinical trial comparing inpatient and outpatient psychotherapy for cluster C PD. To overcome the problem of selection bias, we controlled for initial differences in patient characteristics with the propensity score method.[32]

It can be concluded from our model-based analysis that outpatient psychotherapy and day hospital psychotherapy are the optimal treatments for patients with cluster B PD in terms of cost per recovered patient-year and cost per QALY. The ultimate selection depends on what cost-effectiveness threshold is considered acceptable and what perspective is adopted. The decision whether or not to adopt a treatment strategy is inevitably made in a context of uncertainty surrounding the cost-effectiveness of these strategies, and therefore there is a possibility of making a wrong decision on a patient level. Future work should include a so-called value of information analysis which evaluates the extent to which additional evidence might reduce the probability and the consequences (costs) of a wrong decision and compares that improvement with the cost of information.

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Cost-effective Psychotherapy for Personality Disorders in The Netherlands: the Value of Further Research and Active Implementation

Chapter 6

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Submitted for publication

Abstract

Background

In a budget-constrained health care system, decisions regarding resource allocation towards research and implementation are critical and can be informed by cost-effectiveness analysis.

Aims

The objective of this study was to assess the societal value of conducting further research to inform reimbursement decisions and implementation of cost-effective treatment strategies for cluster B and C personality disorders (PD).

Method

Value of information and value of implementation analyses were conducted using previously developed cost-effectiveness models for cluster B and C PD to evaluate the parameters that contribute to most of the decision uncertainty, and to calculate the population expected values of perfect information (pEVPI) and perfect implementation (pEVPIM).

Results

The pEVPI was estimated to be €613 million for cluster B PD and €587 million for cluster C PD, indicating that gathering additional evidence is expected to be cost-effective. The categories of parameters for which reduction of uncertainty would be most valuable were treatment costs and transition probabilities. The pEVPIM was estimated to be €613 million for cluster B PD and €1,358 million for cluster C PD, suggesting that investing in implementation of cost-effective treatment strategies is likely to be worthwhile.

Conclusions

The societal value of additional research on treatments for cluster B and C PD is substantial, especially when prioritizing information on treatment costs and transition probabilities. Active implementation of cost-effective treatment strategies into clinical practice is likely to improve the efficiency of health-care provision in The Netherlands.

Introduction

Cost-effectiveness analyses are increasingly being used to inform policy decisions regarding the adoption and reimbursement of mental health interventions. Recently, two decision-analytic modeling studies evaluated the cost-effectiveness of various modalities of psychotherapy in treating cluster B personality disorders (PD),[1] including borderline, antisocial, histrionic, and narcissistic PD, and cluster C PD,[2] including avoidant, dependent, and obsessive-compulsive PD. Results indicate that, at a societal willingness-to-pay of €40,000 per QALY, outpatient psychotherapy is the optimal treatment for patients with cluster B PD, while short-term inpatient psychotherapy is the most cost-effective choice for patients with cluster C PD. In other words, if the objective of the health care system is to maximize gains in health outcome subject to a budget constraint, these treatment strategies are, on average, expected to generate the highest level of net benefit and should be adopted.

The decision of whether or not to adopt a treatment strategy is unavoidably subject to uncertainty, as current information on costs and effects is rarely perfect or complete. If the decision based on existing information turns out to be wrong, there will be costs in terms of health benefit and resources forgone, because patients are assigned to suboptimal treatment strategies. An important question, therefore, is whether more information regarding these decisions is desirable.[3] Gathering additional evidence for uncertain parameters is valuable as it is expected to reduce decision uncertainty and thus the probability and the net consequences of a wrong decision; however, is not without costs.

Although our evidence-based findings of cost-effective care in treating personality disorders can inform recommendations for clinical guidelines, it does not guarantee diffusion into clinical practice. This imperfect translation into clinical routines may be due to limited availability in settings where patient demand exceeds treatment capacity. Moreover, it is unlikely that clinicians will immediately alter their professional practice once a treatment is identified as cost-effective.[4] Adherence to suboptimal treatment strategies will compromise the efficiency of health-care provision, resulting in health and resources forgone.[5] Resources need to be allocated toward active implementation of cost-effective treatment strategies using activities such as restructuring and planning of care or education and training of professionals.

Cost-effective health care policy involves making decisions about the reimbursement of cost-effective treatments as well as weighing the potential value of collecting additional evidence and implementation efforts against the costs of these activities. Adequate priority setting and efficient resource allocation thus requires an integral economic analysis of these separate but related options to improve care.

This study aims to establish if additional information would alter our recent findings on the most cost-effective treatment strategies for cluster B and cluster C PD and, if so, which type of research would be most valuable. Additionally, the potential worth of ensuring the implementation of cost-effective care for these patient populations is estimated. We use a single, unified framework that evaluates the uncertainty associated with the adoption decisions to estimate both the value of information and the value of implementation.[6,7] The findings from our study can be used to inform policy debates regarding the efficient allocation of health-care resources among health care provision, research funding, and investments in implementation strategies.

Methods

Patient population and empiric data

Based on the prevalence of cluster C PD in the population of the Netherlands (median of 4.2%; avoidant PD 1.4%, dependent PD 0.8%, and obsessive-compulsive PD 2.0%),[8] the percentage of treatment seeking PD patients (19.1%),[9] and the percentage of PD patients receiving psychotherapy (16.4%),[9] we estimated the annual cluster C PD population eligible for treatment to be 21,546 patients. The various modalities of psychotherapy in treating cluster C PD include long-term outpatient psychotherapy, short-term and long-term day hospital psychotherapy, and short-term and long-term inpatient psychotherapy.

For cluster B PD (median of 6.0%; borderline PD 1.5%, antisocial PD 2.6%, histrionic PD 1.8%, and narcissistic PD 0.1%),[8] we assumed the eligible patients per annum to be 30,780. Treatment options include outpatient psychotherapy, day hospital psychotherapy and inpatient psychotherapy.

Cost-effectiveness analysis and decision uncertainty

Cost-effectiveness analyses were previously conducted using a Markov cohort model based on second-order Monte Carlo simulation.[10] Results were reported from the societal perspective over a five-year time horizon and in terms of costs per quality-adjusted life-year (QALY) gained. The model simulates a cohort of patients that transition through five mutually exclusive health states that represent important attributes of disease. These health states include: (1) recovered; (2) improved; (3) unchanged; (4) relapsed or deteriorated; and (5) death. The model is used to assess the impact of different modalities of psychotherapy on the costs and health outcomes of the patient population over time.

Model parameters were obtained from patient-level data from the largest existing clinical trial of psychotherapy for PD (the SCEPTRE trial), including over 900 patients. Each parameter was assigned a distribution of values in order to characterize the uncertainty in the data (e.g., gamma distributions for costs, and beta distributions for utilities). We assumed probability parameters followed a Dirichlet distribution, a continuous distribution that is the multivariate generalization of the beta distribution. Estimates for the level of implementation were derived by the proportion of the SCEPTRE patient base that received the treatment. Details of model design and analyses have been described in previous publications.[1,2]

In order to explore parameter uncertainty of the model inputs, probabilistic sensitivity analysis was conducted by randomly sampling from each of the parameter distributions and calculating the expected costs, and expected QALYs for each treatment strategy using that combination of parameter values in the model. This process was replicated one thousand times (i.e., second-order Monte Carlo simulation) for each treatment option resulting in the expected cost-effectiveness. Decision uncertainty is represented in the cost-effectiveness acceptability frontiers (CEAF),[11] which plot the probability that the treatment strategy with the maximum expected net monetary benefit is in fact the most cost-effective over a range of threshold values. As reported previously, we found that outpatient psychotherapy was the most cost-effective treatment for cluster B PD and short-term inpatient psychotherapy for cluster C PD at a threshold of €40,000 per QALY.

Value of information and value of implementation analysis

To explore both the value of information and the value of implementation we used a framework matrix developed by Fenwick and colleagues[6] representing a four-state world where both information and implementation can be either at the current level or perfect (**Table 6.1**). By subtracting the expected values for different states, the maximum societal values associated with further research and implementation efforts can be calculated. These upper bound estimates should be weighed against the costs of these activities to determine whether they are worthwhile.

Expected value of perfect information – Compared to information at the current level about the costs and effects of the different treatment strategies for PD, perfect information would eliminate the possibility of making the wrong reimbursement decision. The EVPI can be interpreted as the maximum that the health care system would be willing to pay for additional evidence to inform the reimbursement decision in the future, and it places an upper bound on the value of conducting further research. For both cluster B and cluster C cost-effectiveness analyses, the expected value of perfect information (EVPI) was calculated by taking the difference between the expected net benefit with perfect information (cell D in **Table 6.1**) and the expected net benefit with current information (cell C in **Table 6.1**).

Table 6.1 Framework matrix for determining the expected value of perfect information and of perfect implementation (Fenwick et al., 2008)

	Information	
Implementation	Current	Perfect
Current	A	B
Perfect	C	D

Expected value of partial perfect information – The expected value of partial perfect information (EVPPI) identifies the input parameters in the decision model that contribute to most of the decision uncertainty and for which future research is most valuable.

The model parameters were grouped into four subsets to match the type of research that would be conducted: (1) transition probabilities between health states, (2) treatment costs of the different modalities of psychotherapy, (3) health state costs, which reflect the costs of health care utilization and productivity losses incurred by patients in each state, and (4) health state utilities, which reflect the health-related quality of life experienced by patients in each state. The EVPPI for the parameter groups was calculated with a similar approach as for EVPI by taking the difference between the expected value of a decision made with perfect and current information about the parameters.

Expected value of perfect implementation – The current, imperfect implementation of cost-effective treatment strategies into clinical practice compromises the expected efficiency of patient management in terms of health benefits and resources forgone. As such, there is value in actively ensuring the implementation of cost-effective clinical guidelines. The expected value of perfect

implementation (EVPIM) provides a measure of the upper bound of the value of implementation efforts to change capacity of and adherence to cost-effective treatment strategies. For both cluster B and cluster C cost-effectiveness analyses, the EVPIM was calculated by taking the difference between the expected net benefit with perfect implementation (cell C in **Table 6.1**) and the expected net benefit with implementation at its current level (cell A in **Table 6.1**). Net monetary benefits for the expected value with current implementation were calculated by taking the weighted average of the expected net benefit with perfect implementation (and current information), where the weights reflect the current level of implementation.

Expected value of perfection – The expected value of perfection (EVP) is a combined measure of the maximum possible return to resources expended on research and implementation strategies. The EVP was calculated by taking the difference between the expected net benefit with both perfect information and implementation (cell D in **Table 6.1**) and the expected net benefit with information and implementation at its current level (cell A in **Table 6.1**).

Because information and implementation are expected to serve the public domain, the EVPI, EVPPI, EVPIM and EVP were calculated at the population level by multiplying the patient-level values by the number of patients who will receive psychotherapy over the assumed time horizon for the intervention. Cases were discounted at an annual rate of 4.0%, consistent with guidelines for economic evaluations in the Netherlands.[12]

Base case and sensitivity analysis

In the base case analyses, a societal willingness-to-pay threshold value of €40,000 per QALY was used. The expected lifetime of psychotherapy was assumed to be 5 years.

In sensitivity analyses, the decision uncertainty, population EVPI, EVPIM and EVP were calculated for different values of the threshold. In addition, we studied the impact of the current level of implementation and the size of the eligible patient population on the expected population values of information and implementation.

In all analyses, the expected population values were calculated across 1000 Monte Carlo simulations with 1000 draws from the parameter group of interest.

Results

Base case analysis

Table 6.2 summarizes the currently available evidence on the costs and effects of the five alternative treatment dosages of psychotherapy for cluster C PD and three psychotherapy modalities for cluster B PD, and denotes the most cost-effective choice (i.e., the option with the highest incremental cost-effectiveness ratio (ICER) below the threshold, or the option that maximizes net monetary benefit) at a willingness-to-pay threshold of € 40,000 per QALY. With current information, short-term inpatient psychotherapy for cluster C PD is the optimal decision as this intervention generates the highest expected net benefit (€51,124 at a threshold of €40,000 per QALY). The probability that short-term inpatient psychotherapy is indeed cost-effective is only 0.52 and thus there is value in reducing the error probability of 0.48 by collecting additional evidence. Assuming implementation is perfect, the expected value of perfect information for individual patients is €5,884 over a five-year time horizon; with 99,756 eligible patients in the population, the population expected value of perfect information (pEVPI) is €587 million (**Table 6.3**).

Table 6.2 Cost-effectiveness results over five-years (Soeteman et al., in press; Soeteman et al., 2010)

		Cluster C PD		
Psychotherapy dosage	**Cost**	**QALY**	**ICER#**	**NMB***
Short-term day hospital	€ 89,411	3.44	—	€ 48,001
Long-term outpatient	€ 89,936	3.30	dominated	€ 42,135
Short-term inpatient	€ 91,620	3.57	€ 16,570	€ 51,124
Long-term day hospital	€ 105,940	3.49	dominated	€ 33,670
Long-term inpatient	€ 119,946	3.49	dominated	€ 19,731
		Cluster B PD		
Modality of psychotherapy	**Cost**	**QALY**	**ICER#**	**NMB***
Outpatient	€ 80,247	3.11	—	€ 44,072
Day hospital	€ 91,090	3.30	€ 56,325	€ 40,929
Inpatient	€ 97,351	3.32	€ 286,493	€ 35,542

Incremental cost-effectiveness ratios (ICER) were calculated as the difference in cost divided by the difference in QALYs between the strategy and the next best non-dominated strategy. The option with the highest ICER below the threshold of €40,000 per QALY is the most cost-effective choice.

* Net monetary benefit (NMB) was calculated by multiplying QALYs by the threshold value of €40,000 per QALY and subtracting cost. The strategy with the maximum NMB is the most cost-effective choice.

Table 6.3 Framework matrix for short-term inpatient psychotherapy in treating cluster C PD

For individual patients (€)

	Information	
Implementation	**Current**	**Perfect**
Current	37,515 (A)	37,515 (B)
Perfect	51,124 (C)	57,007 (D)

For the total eligible population (€ millions)

	Information	
Implementation	**Current**	**Perfect**
Current	3,742 (E)	3,742 (F)
Perfect	5,100 (G)	5,687 (H)

Societal willingness-to-pay per QALY	€ 40,000
Total eligible population over 5 years	99,756
EVPI for patient = D - C =	€ 5,884
pEVPI (in million) = H - G =	€ 587
EVPIM for patient = C - A =	€ 13,609
pEVPIM (in million) = G - E =	€ 1,358
EVP for patient = D - A =	€ 19,492
pEVP (in million) = H - E =	€ 1,944

With 63 out of 448 cluster C patients of the SCEPTRE population receiving short-term inpatient psychotherapy, we assumed the current level of implementation to be 0.141. Likewise, for long-term outpatient psychotherapy, short-term and long-term day hospital psychotherapy, and long-term inpatient psychotherapy the current level of implementation was estimated to be 0.214, 0.190, 0.230, and 0.225, respectively. Based on the current level of information, the expected value of perfect implementation for individual patients is €13,609 over a five-year time horizon; with 99,756 eligible patients in the population, the population expected value of perfect implementation (pEVPIM) is €1,358 million.

Likewise, outpatient psychotherapy provides the highest expected net benefit for cluster B PD (€44,072 at a threshold of €40,000 per QALY). The probability that outpatient psychotherapy is cost-effective is 0.51; in that case the expected value of perfect information for individual patients is €4,303 over a five-year time horizon and the population expected value of perfect information (pEVPI) is €613 million (**Table 6.4**).

Table 6.4 Framework matrix for outpatient psychotherapy in treating cluster B PD

For individual patients (€)

	Information	
Implementation	**Current**	**Perfect**
Current	39,772 (A)	39,772 (B)
Perfect	44,072 (C)	48,375 (D)

For the total eligible population (€ millions)

	Information	
Implementation	**Current**	**Perfect**
Current	5,668 (E)	5,668 (F)
Perfect	6,281 (G)	6,894 (H)

Societal willingness-to-pay per QALY	€ 40,000
Total eligible population over 5 years	142,508
EVPI for patient = D - C =	€ 4,303
pEVPI (in million) = H - G =	€ 613
EVPIM for patient = C - A =	€ 4,300
pEVPIM (in million) = G - E =	€ 613
EVP for patient = D - A =	€ 8,603
pEVP (in million) = H - E =	€ 1,226

The SCEPTRE trial showed that 57 out of 241 patients received outpatient psychotherapy, and therefore we assumed the current level of implementation was 0.237. For day hospital psychotherapy and inpatient psychotherapy the current level of implementation was estimated to be 0.411 and 0.353, respectively. Based on the current level of information, the expected value of perfect implementation for individual patients is €4,300 over a five-year time horizon and €613 million for the eligible population (pEVPIM).

The population expected value of perfection (pEVP) was €1,944 million for cluster C PD (€19,492 for individual patients) (**Table 6.3**) and €1,226 million for cluster B PD (€8,603 for individual patients) (**Table 6.4**), suggesting that there is considerable scope for improving the efficiency of health care provision for cluster B and cluster C PD patients.

Figure 6.1 Population expected value of partial perfect information (pEVPPI) at a cost-effectiveness threshold of €40,000 per QALY and assuming a five-year lifetime for psychotherapy. A, pEVPPI for cluster C PD. B, pEVPPI for cluster B PD.

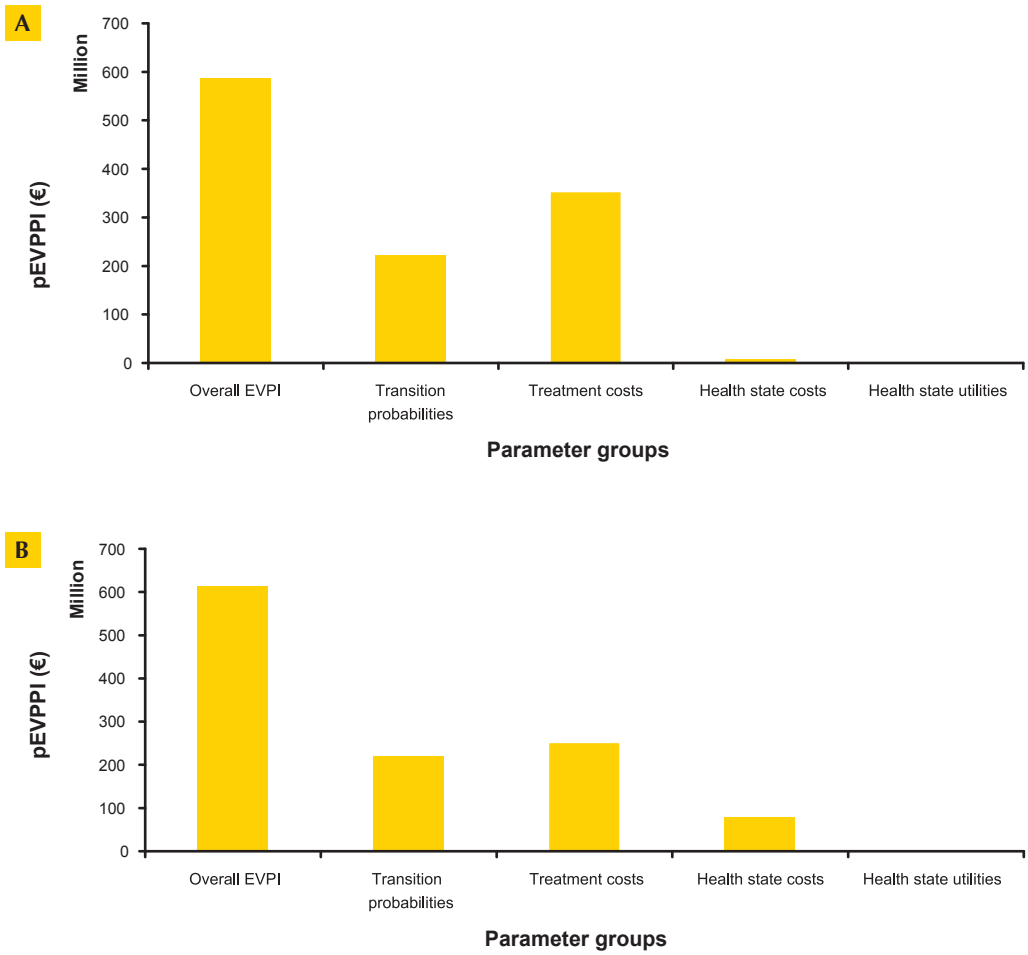
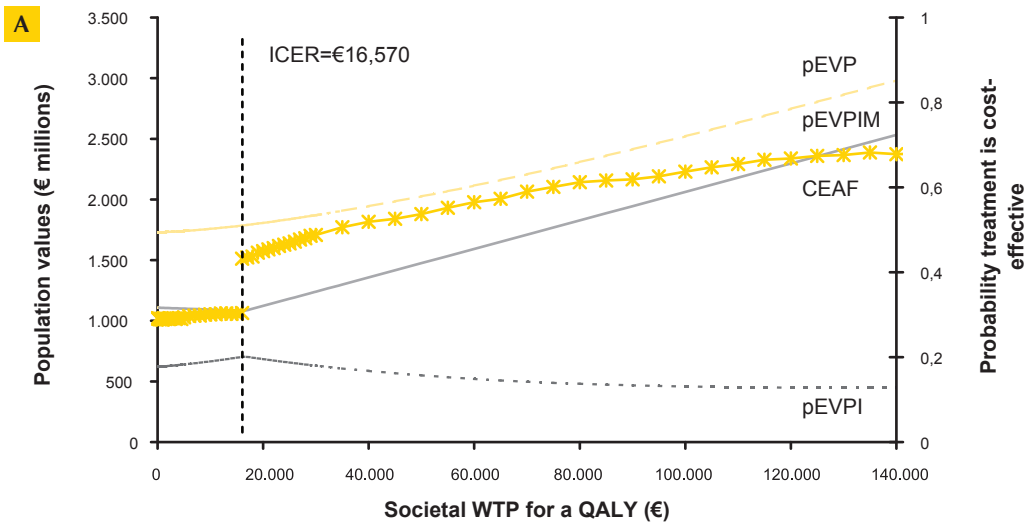


Figure 6.1 (A) displays the population expected value of partial perfect information (pEVPPI) for the four groups of parameters at a cost-effectiveness threshold of €40,000 per QALY and a five-year lifetime for psychotherapy. The pEVPPI associated with treatment costs and tran-

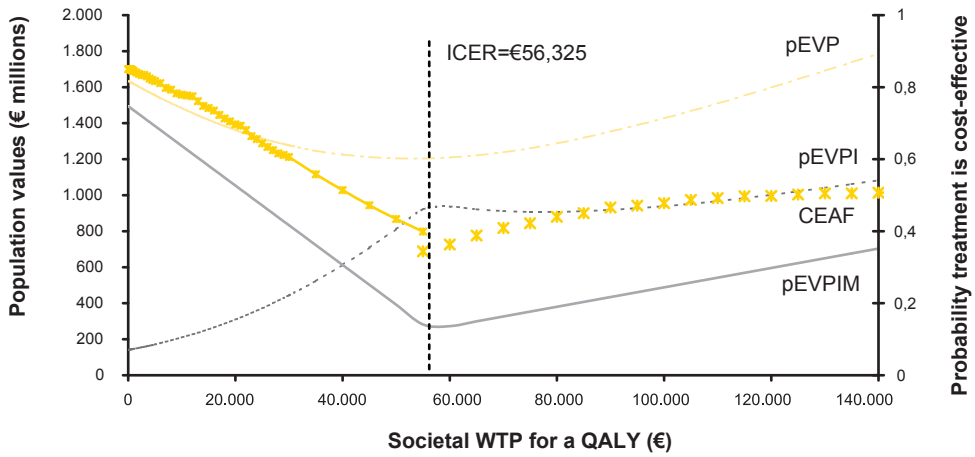
sition probabilities are relatively high; research that would eliminate the uncertainty in these subsets of parameters would be worth €352 million and €222 million, respectively (€3,529 and €2,227 for individual patients). In contrast, the model input parameters related to health state costs have lower value of information (€8 million or €80 for individual patients), and health state utilities have no value of information (€0). Note that the pEVPPI for the groups of parameters do not sum to the overall pEVPI for the model, attributable to the interactions within the model structure.

Figure 6.1 (B) shows that the pattern of partial EVPI for cluster B PD is very similar to that of cluster C PD, with relatively high values associated with treatment costs and transition probabilities (pEVPPI of €250 million and €219 million, respectively; €1,754 and €1,537 for individual patients). The value of information associated with health state costs is much lower (€79 million; €557 for individual patients) and the value associated with health state utilities is zero.

Figure 6.2 Population expected values of perfect information (pEVPI), perfect implementation (pEVPIM), and perfection (pEVP) (primary axis) and cost-effectiveness acceptability frontier (CEAF) (secondary axis) as a function of the societal WTP for the adoption decision regarding: A, the five treatment strategies for cluster C PD. B, the three treatment strategies for cluster B PD.



B



Sensitivity analysis

Level of the societal willingness-to-pay per QALY – **Figure 6.2 (A)** illustrates the relationship between the CEAF, pEVPI, pEVPIM, and pEVP and the societal willingness-to-pay per QALY for the adoption decision regarding the five plausible treatment strategies for cluster C PD. The extent of uncertainty surrounding the decision is formally quantified in the pEVPI curve. This curve initially increases as the cost-effectiveness threshold rises, with a local maximum occurring at the value corresponding to the incremental cost-effectiveness ratio (ICER) of €16,570 per QALY; at this point the optimal option changed from short-term day hospital psychotherapy to short-term inpatient psychotherapy and the choice between strategies is most uncertain (illustrated by the relatively low CEAF values). The pEVPI curve decreases when the threshold is higher than the ICER, suggesting that the falling probability of error of the decision to adopt short-term inpatient psychotherapy (reflected by the CEAF) offsets the value of the consequences of error, which are valued more highly at higher thresholds.

Indicating the maximum return to investments in implementation, the pEVPIM curve initially decreases as the cost-effectiveness threshold rises with a local minimum occurring at the value that corresponds to the ICER. At this point decision makers are indifferent about which of the cost-effective strategies are implemented. The value is, however, not zero because there is value to be gained from reducing the current adherence to suboptimal treatment options, i.e. long-term day hospital psychotherapy and long-term inpatient psychotherapy. The pEVPIM curve rises for threshold values above the ICER as a result of the increasing value to be gained from implementing short-term inpatient psychotherapy, which is identified (with increasing certainty) as the optimal treatment strategy.

The pEVP curve can be derived by summing pEVPI and pEVPIM and displays a gradually increase over the full range of threshold values.

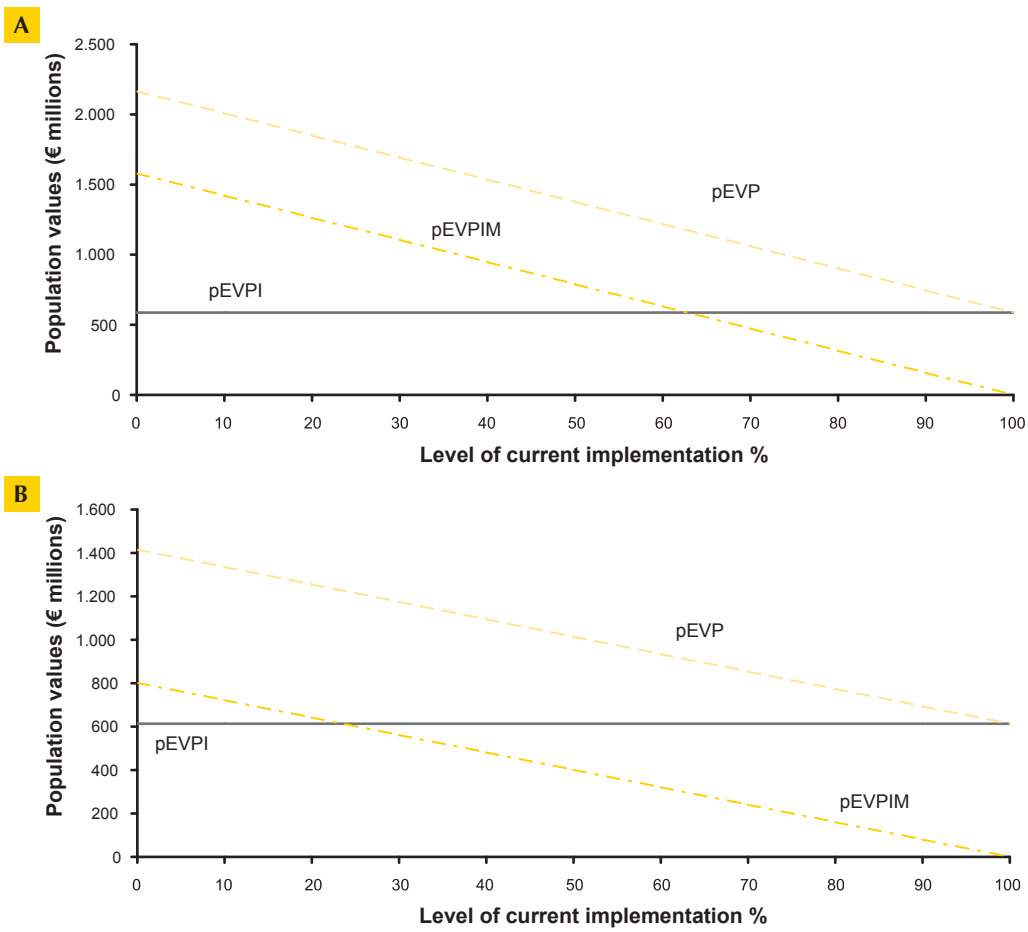
Figure 6.2 (B) shows the CEAF, pEVPI, pEVPIM, and pEVP as a function of the cost-effectiveness threshold for the adoption decision regarding the three possible treatment strategies for cluster B PD. Initially, the pEVPI values are relatively low and the pEVPIM values relatively high, indicating that there is not much uncertainty surrounding the adoption of outpatient psychotherapy reflected by high values associated with strategies to change implementation. The steep pEVPIM curve reaches a minimum and the pEVPI curve a maximum when the threshold equals the ICER of €56,325 per QALY where there is a change in the optimal treatment strategy from outpatient psychotherapy to day hospital psychotherapy. At this point the probability of making a wrong decision is relatively high (illustrated by the relatively low CEAF values) and policy makers are indifferent which treatment to implement. In contrast to the pEVPI for the cluster C analysis, the curve gradually increases when the threshold is higher than the ICER, suggesting that the rise in the value of the consequences of error outweighs the gradually falling probability of error of the decision to adopt short-term day hospital psychotherapy (reflected by the CEAF).

The U-shaped pEVP curve shows that with increasing threshold values, there is alternately less, equal, and more potential value associated with research funding than with investments in implementation.

Level of current implementation – **Figure 6.3** displays the impact of the level of current implementation on the expected population values of information (pEVPI), implementation (pEVPIM), and perfection (pEVP). At a cost-effectiveness threshold of €40,000 per QALY, outpatient psychotherapy for cluster B PD and short-term inpatient psychotherapy for cluster C PD are the most cost-effective treatment strategies and the optimal level of implementation would be 1. When the current level of implementation is 1, the pEVPIM is 0 because all patients are receiving the most cost-effective treatment. When the current level of implementation is 0, the pEVPIM is €1,580 million for cluster C PD (**Figure 6.3 (A)**) and €802 million for cluster B PD (**Figure 6.3 (B)**). With an increasing level of current implementation, the pEVPIM curve decreases as more patients will receive the optimal treatment and strategies to change implementation have less value. The level of implementation has no impact on the pEVPI, because we assumed perfect implementation. The pEVP curve decreases with increasing level of current implementation.

Size of the eligible population – The size of the eligible patient population has a direct impact on the population-level estimates of the pEVPI, pEVPIM, and pEVP (not shown). With increasing size of the eligible patient population per annum, the population expected values are increasing.

Figure 6.3 Population expected values of perfect information (pEVPI), perfect implementation (pEVPIM), and perfection (pEVP) as a function of the level of current implementation of the most cost-effective treatment at a threshold of €40,000 per QALY. A, short-term inpatient psychotherapy for cluster C PD. B, outpatient psychotherapy for cluster B PD.



Discussion

Extending from previous cost-effectiveness analyses, we estimated the societal value of conducting additional research related to the adoption decisions of cost-effective treatment strategies for cluster B and cluster C PD. To our knowledge, this is the first formal measure of value of information regarding mental health interventions. It is important to note that, although health care systems invest heavily in research, research prioritization is generally not based on a unified

and coherent framework. Moreover, we used value of implementation analysis to determine the potential worth of implementing these cost-effective treatment strategies into clinical practice. Therefore, this study has the potential to contribute significantly to the knowledge base guiding rational decision making of allocation of health care resources across health care provision, research funding, and implementation investments within and between broad clinical areas.

Our findings indicate that the societal value of additional research is substantial, estimated at €613 million for cluster B PD and €587 million for cluster C PD, assuming a willingness-to-pay threshold of €40,000 per QALY and a five-year lifetime for psychotherapy. The expected value of partial perfect information associated with the model parameters (EVPPI) indicate that more evidence about treatment costs and transition probabilities between health states would be most valuable, while additional evidence about health state costs and health state utilities would be of relatively little or no value. Considering the current level of implementation of cost-effective treatment strategies in clinical practice and a threshold value of €40,000 per QALY, there is substantial societal benefit in changing the capacity of and adherence to cost-effective treatment strategies, with the expected population value of perfect implementation (EVPIM) estimated to be €613 million for cluster B PD and €1,358 million for cluster C PD.

From a policy perspective, we recommend reimbursement of outpatient psychotherapy for cluster B PD and short-term inpatient psychotherapy for cluster C PD while simultaneously commissioning further research and active implementation of cost-effective treatments in order to more efficiently allocate health care resources.

Our calculations were based on the assumption that the level of implementation was independent of the level of information, which in reality may not be the case as the amount of information available alters the implementation effort. Moreover, the calculated upper bound estimates should be weighed against the costs of these activities to determine whether they are potentially worthwhile. It is likely that implementation strategies will be more costly than further research. Therefore, for cluster C PD, we do not recommend implementation without further research even though more value was associated with strategies to change implementation (EVPIM=€1,358 million) than with further research (EVPI=€587).

The expected population values of information (pEVPI), implementation (pEVPIM), and perfection (pEVP) are greatly affected by the level of current implementation, the size of the eligible patient population, and the societal willingness-to-pay per QALY. As a result, policy recommendations between technologies can differ substantially.

Although the expected value of perfect information (EVPI) analyses suggest that further research may be justified to support the future adoption decisions of cost-effective treatment strategies for cluster B and cluster C PD, the partial EVPI analyses for the four groups of parameters indicate that this may not require an experimental design. More precise estimates of treatment costs and health state costs, which account for 60% (cluster B model) and 62% (cluster C model) of the value of additional information, can be acquired without an additional clinical trial and can instead be based on an observational survey. In addition, conducting an observational study may be more feasible if patients are reluctant to participate in a trial in which they are randomly assigned to different psychotherapy treatment groups, as was the experience of the SCEPTRE study group in the case of cluster C PD patients. Thus, although additional evidence about transition probabilities is valuable, gathering information on treatment costs and health state costs may be preferred, considering the study design required is less costly and much more feasible in this particular patient population compared to a randomized controlled trial.

In prioritizing research, the expected societal value of €613 million for cluster B PD and €587 million for cluster C PD should be compared with the expected societal value of other proposed clinical research projects. The value of psychotherapy research for PD falls comfortably within the results of a pilot study summarizing the evidence of six case studies evaluating value of information ranging from £2,8 million (liquid based cytology screening for cervical cancer) and £865 million (clopidogrel and dipyridamole in the secondary prevention of occlusive vascular events).[13]

A major strength of this study is its use of an integral approach of state of the art decision-analytic methods to identify priority areas for mental health care provision, research, and implementation. Literature indicates that measures of the burden of disease have been used to allocate research funds to different clinical areas.[14,15,16] While burden of disease measures can identify priority areas for research, they do not indicate if the research informing a specific clinical decision for a specific group of patients is valuable. Value of information and implementation analysis provide a single framework in which the most cost-effective research as well as implementation strategies can be identified and is thus consistent with society's goal of maximizing health gain given a budget constraint.

Our analysis has a number of limitations. First of all, in our EVPIM analysis, we optimistically assumed that the current level of implementation for outpatient psychotherapy for cluster B PD is 0.237, and for short-term inpatient psychotherapy for cluster C PD is 0.141. To the extent that the current level of implementation based on the SCEPTRE data is highly influenced by a selection of mental health institutions that are relatively highly specialized, our results could be considered conservative. Considering the true capacity for the Netherlands to provide specialized treatments to PD patients may be much lower, the societal value of implementing these treatment strategies is likely much higher. In addition, the five-year expected lifetime for psychotherapy was chosen rather conservatively. One could argue that the lifetime for psychotherapy may be much longer and that there may be more future patients who can benefit from the additional evidence, resulting in an even higher societal benefit of further research.

Secondly, much of the data needed to calculate the total eligible population for PD treatment (e.g. prevalence rates, percentage of treatment seeking PD patients, percentage of PD patients receiving psychotherapy) are not available for the Netherlands, therefore we relied on data from other settings. Furthermore, while we calculated the maximum value associated with further research and changing clinical practice, we did not consider the expected costs of additional research or the expected costs of implementation to determine whether these activities are in fact worthwhile. Finally, inherent to the assessment of the expected value of perfect information and the expected value of perfect implementation, information is rarely perfect. Therefore, the expected value of sample information (EVSI) and the expected value of specific implementation (EVSIM) can be calculated indicating the societal value of information from specific research or of specific implementation strategies. Future research should include such analyses.

Despite these limitations, our findings suggest that the societal value of additional research on treatments for cluster B and C PD is substantial, particularly when prioritizing information on treatment costs and transition probabilities. Furthermore, implementing these cost-effective treatment strategies into clinical practice is likely to improve the efficiency of health-care provision in the Netherlands.

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General discussion

Using state of the art decision-analytic methods this dissertation provides insights into three questions that need to be addressed by any health care system in order to optimize allocation of health care resources: (1) Based on currently available evidence, how cost-effective is it to reimburse a health intervention?, (2) Is it cost-effective to fund research to collect further evidence to inform the reimbursement decision in the future?, and (3) Is it cost-effective to invest in active implementation of the cost-effective health interventions?

Personality disorders are common in the general population and mental healthcare settings, are associated with a low quality of life, and pose high costs to society. Effective treatments are available but can have exceedingly high costs. To address the first question we conducted two decision-analytic modeling studies, as part of the Study on the Cost-Effectiveness of Personality disorder TREatment (SCEPTRE), which evaluated the cost-effectiveness of various modalities of psychotherapy in treating cluster B personality disorders, including borderline, antisocial, histrionic, and narcissistic personality disorders, and cluster C personality disorders, including avoidant, dependent, and obsessive-compulsive personality disorders. Results indicated that, based on currently available evidence, cost-effective treatment strategies are indeed available. At a societal willingness to pay of €40,000 per QALY, outpatient psychotherapy for cluster B personality disorders and short-term inpatient psychotherapy for cluster C personality disorders can be considered the most cost-effective choice. In order to provide insights into the second and third question and extending from these cost-effectiveness analyses, the maximum return on investments in additional research and implementation efforts was explored. Results suggested that there was substantial value associated with further research, especially when prioritizing information on treatment costs and transition probabilities, and with implementing the cost-effective treatments into clinical practice. From a policy perspective, therefore, we recommend reimbursement of outpatient psychotherapy for cluster B personality disorders and short-term inpatient psychotherapy for cluster C personality disorders while simultaneously commissioning further research and active implementation of cost-effective treatments in order to more efficiently allocate health care resources.

Implications for patients with personality disorders seen in clinical practice

The economic evidence provided by this work can inform recommendations for clinical guidelines. The SCEPTRE patient population is broadly representative of treatment-seeking adult patients with personality disorders and thus the results should be broadly applicable to those patients who are evaluated and treated as part of routine clinical practice.

The first challenge by clinicians in interpreting our results, however, may be in identifying the optimal strategy at the individual (patient) level, and a tension may arise when the clinical judgment conflicts with the policy recommendations. The decision-analytic approach in these studies is intended to inform recommendations from the public health (i.e., population) perspective and is not inherently designed to inform decision making at the individual level. Although we used primary patient-level data from a clinical study, we used those data to inform population averages (and plausible ranges) for our parameters. As a result, we were limited in our ability to examine individual-level heterogeneity such that, for example, there will undoubtedly be some patients with cluster C personality disorder for whom long-term inpatient psychotherapy may be the best suited option, even though it was not a cost-effective option in our analysis.

Secondly, we find it important to emphasize that cost-effectiveness is only one aspect that influences decision making; another important factor that was not considered in this dis-

sertation is affordability. Decision-makers are constrained by a fixed budget and may not be able to fund the new recommendations if it means that more patients are allocated to more expensive treatment strategies, even if these strategies are the most cost-effective choice. Therefore, the impact of these recommendations on the total health care budget should be explored.

Despite these modifications inherent to the use of economic evaluation for decision making, this work has the potential to contribute significantly to the knowledge base guiding rational decision making in order to optimize allocation of health care resources across health care provision, research funding, and implementation investments within and between broad clinical areas.

Recommendations for future research

In clinical decision making, there is indeed an increasing recognition that every patient is unique. In policy decision making, however, there is a strong focus on parameter uncertainty thereby neglecting the potential influence of individual-level heterogeneity on the decision uncertainty. Subgroup analyses may demonstrate the potential for the resulting cost-effectiveness to vary across individuals with different characteristics (e.g., personality disorder types, severity of pathology, etc). Another approach to acknowledge heterogeneity within economic evaluations and the decision making framework is first-order Monte Carlo simulation and discrete event simulation (DES). In contrast to the second-order Monte Carlo simulation we conducted, these two approaches sample one patient at a time allowing for consideration of important patient-specific sociodemographic characteristics and individual variation of disease history. Importantly, the DES method deviates from the fixed time assumption required in Markov models, allowing for reflection of time to event that may vary from patient to patient, either stochastically or because of an individual's prior history. The SCEPTRE trial would be particularly suitable for a DES analysis because of the large primary patient level data set available.

Sample size calculation plays an important role in clinical research. Although our work identifies priority areas for further research (treatment costs and transition probabilities) from a Bayesian perspective, calculating the optimal sample size was beyond the scope of our research. The Bayesian approach for calculating sample sizes is more informative than the traditional power calculation based on the frequentist approach. By weighing the expected value of sample information (EVSI) against the costs of proposed research, the Bayesian approach identifies the optimal sample size at the point at which the expected net benefit of sampling (ENBS) reaches a maximum. In the frequentist analysis, only effect-sizes play a role and no costs are taken into account. For small effects, the enormous costs of the sample size required to detect rare events would be virtually ignored. Generally, sample sizes are therefore chosen rather arbitrarily to achieve finite and manageable numbers. Extending on our Bayesian analyses, the optimal sample size should be explored to identify the most efficient research design.

Finally, data on incidence of personality disorders, prevalence rates in the general population, percentage of treatment-seeking patients, and percentage of patients receiving psychotherapy are not available for The Netherlands. Therefore, personality disorders should be prioritized on the research agenda and included in studies such as The Netherlands Mental Health Survey and Incidence Study (NEMESIS).

Conclusions

Especially in current times of health care reform and economic crisis, when the affordability of health coverage is scrutinized, the awareness among citizens is building that society has to take great care in spending its money prudently. More studies are needed to weigh the costs of health interventions, performing additional research, and active implementation against the societal benefits, especially in mental health care. The trade off is simple: if we save money by treating personality disorders, conducting further research, and actively implementing cost-effective treatment strategies, then we have invested our money wisely. This line of reasoning, while traditionally at odds with clinical practice, is increasingly becoming reality. The challenge thus will be to communicate these novel methods of and findings from decision science to the general audience.

Finally, decision models can be iteratively updated with the addition of new information from future studies. Indeed, our aim is to refine our model, revisit our inputs, and revise the analyses as more information becomes available to continue to inform decisions with the best available data. Until then and based on the totality of the available evidence, we conclude that the burden of disease in treatment-seeking adult patients with personality disorders is high, that cost-effective treatment strategies are available, and that further research for and implementation of the cost-effective treatments are valuable to society.

Summary

Using state of the art decision-analytic methods this dissertation provides insights into three questions that need to be addressed by any health care system in order to optimize allocation of health care resources: (1) Based on currently available evidence, how cost-effective is it to reimburse a health intervention?, (2) Is it cost-effective to fund research to collect further evidence to inform the reimbursement decision in the future?, and (3) Is it cost-effective to invest in active implementation of the cost-effective health interventions?

The aim of the first two dissertation chapters was to investigate the burden of disease among treatment-seeking personality disorder patients in terms of quality of life (Chapter 2) and societal costs (Chapter 3). We studied the quality of life among the 1,708 patients included in the Study on the Cost-Effectiveness of Personality disorder TREatment (SCEPTRE) from six mental health care institutes in The Netherlands. Our results show that patients with a DSM-IV diagnosis of personality disorder experience a low quality of life with an EQ-5D index value of .56, commensurate with physical disorders such as rheumatic disease, lung cancer, or Parkinson's disease. Our results also suggest that from the patient perspective, the primary focus of scientific attention on borderline personality disorder should shift to dependent, paranoid, narcissistic, schizoid, depressive, histrionic, self-defeating, and negativistic personality disorders given the higher burden with respect to diminished quality of life of these conditions.

The second study shows that the same population of treatment-seeking patients with personality disorders impose high costs upon society. The mean total cost in the year prior to treatment was €11,126 per patient. The mean direct medical cost was €7,398 per patient, mainly comprised of costs due to inpatient health care (33.1%) (e.g., admissions into general or psychiatric hospital) and outpatient mental health care (26.1%). The mean indirect cost was €3,728 per patient. Borderline and obsessive-compulsive personality disorders were significant predictors of increased mean total cost. The economic burden of our patient population was substantially higher than the burden among patients with depression and generalized anxiety disorder, and comparable to that in patients with schizophrenia.

When the burden of disease in a patient population is high, society is inclined to pay more for a gain in health benefit (e.g., life year).

The subsequent chapters describe two decision-analytic modeling studies which evaluated the cost-effectiveness of various modalities of psychotherapy in treating cluster C personality disorders (Chapter 4), including avoidant, dependent, and obsessive-compulsive personality disorders, and cluster B personality disorders (Chapter 5), including borderline, antisocial, histrionic, and narcissistic personality disorders. We developed a Markov cohort model to integrate clinical and economic data from the SCEPTRE trial in order to compare the treatment strategies over a five-year time horizon in terms of costs per recovered patient-year and costs per quality-adjusted life year (QALY). Four types of parameters were used in the model: (1) transition probabilities, (2) treatment costs, (3) costs of health care utilization and productivity losses incurred by patients, and (4) health state utilities. Parameter uncertainty was explored by conducting a probabilistic analysis in which distributions were assigned to the input parameters of the model. Results indicate that, based on currently available evidence, cost-effective treatment strategies are indeed available. For cluster C personality disorders, the switch points, at which there is a change in the optimal option from short-term day hospital psychotherapy to short-term inpatient psychotherapy, were located at a threshold value of €2,637 per recovered patient-year and €16,570 per QALY. For cluster B personality disorders, the optimal option changed from outpatient psychotherapy to day hospital psychotherapy and from day hospital psychotherapy

to inpatient psychotherapy, at threshold values of €12,274 and €113,298 per recovered patient-year and €56,325 and €286,493 per QALY. The observed burden of disease among cluster C and cluster B personality disorders indicates that treatments may cost up to about €40,000 per QALY to be acceptable. Based on this cost-effectiveness threshold, outpatient psychotherapy for cluster B personality disorders and short-term inpatient psychotherapy for cluster C personality disorders can be considered the most cost-effective choice in terms of costs per QALY.

Extending from these cost-effectiveness analyses, in Chapter 6, the maximum return on investments in additional research and implementation efforts were explored. Value of information and value of implementation analyses were conducted to evaluate the parameters that contribute to most of the decision uncertainty, and to calculate the expected values of perfect information (EVPI) and perfect implementation (EVPIM). Our findings indicate that the societal value of additional research is substantial, estimated at €613 million for cluster B personality disorders and €587 million for cluster C personality disorders, assuming a cost-effectiveness threshold of €40,000 per QALY and a five-year lifetime for psychotherapy. More evidence about treatment costs and transition probabilities between health states would be most valuable. Considering the current level of implementation of cost-effective treatment strategies in clinical practice, there is substantial societal benefit in changing the capacity of and adherence to cost-effective treatment strategies, with the EVPIM estimated to be €613 million for cluster B personality disorders and €1,358 million for cluster C personality disorders.

From the policy perspective, therefore, we recommend reimbursement of outpatient psychotherapy for cluster B personality disorders and short-term inpatient psychotherapy for cluster C personality disorders while simultaneously commissioning further research and active implementation of cost-effective treatments in order to optimize allocation of health care resources.

Especially in current times of health care reform and economic crisis, when the affordability of health coverage is scrutinized, the awareness among citizens is building that society has to take great care in spending its money prudently. More studies are needed to weigh the costs of health interventions, performing additional research, and active implementation against the societal benefits, especially in mental health care. The trade off is simple: if we save money by treating personality disorders, conducting further research, and actively implementing cost-effective treatment strategies, then we have invested our money wisely. This line of reasoning, while traditionally at odds with clinical practice, is increasingly becoming reality. The challenge thus will be to communicate these novel methods of and findings from decision science to the general audience.

Samenvatting

Door gebruik te maken van geavanceerde besliskundige methoden maakt dit proefschrift drie vragen inzichtelijk die door elk gezondheidszorgstelsel dienen te worden behandeld om de toewijzing van vergoedingen te optimaliseren: (1) Hoe kosteneffectief is het een bepaalde gezondheidsinterventie te vergoeden, gebaseerd op de huidige beschikbare evidentie?, (2) Is het kosteneffectief om verder onderzoek te financieren om daar het vergoedingsbesluit in de toekomst op te kunnen baseren?, en (3) Is het kosteneffectief om te investeren in het actief implementeren van de kosteneffectieve gezondheidsinterventies?

Het doel van de eerste twee hoofdstukken van dit proefschrift was het onderzoeken van de ziektelast onder zorgzoekende patiënten met persoonlijkheidsstoornissen in termen van kwaliteit van leven (Hoofdstuk 2) en maatschappelijke kosten (Hoofdstuk 3). We onderzochten de kwaliteit van leven van 1.708 patiënten die vanuit zes verschillende geestelijke gezondheidszorginstellingen in Nederland werden ingesloten in the SCEPTRE-studie (Study on the Cost-Effectiveness of Personality disorder TREatment). Onze resultaten laten zien dat patiënten die voldoen aan een DSM-IV diagnose van een persoonlijkheidsstoornis een lage kwaliteit van leven ervaren met een EQ-5D index waarde van 0,56, wat van gelijke omvang is als de kwaliteit van leven in lichamelijke stoornissen zoals reuma, longkanker of de ziekte van Parkinson.

Onze resultaten suggereren ook dat vanuit het patiëntenperspectief, de wetenschappelijke focus die nu ligt op de borderlinepersoonlijkheidsstoornis zou moeten verschuiven naar de afhankelijke, paranoïde, narcistische, schizoïde, depressieve, theatrale, zelfondermijnende en negativistische persoonlijkheidsstoornis, gegeven de hogere ziektelast door een verminderde kwaliteit van leven van deze condities.

De tweede studie laat zien dat dezelfde populatie van zorgzoekende patiënten met persoonlijkheidsstoornissen hoge maatschappelijke kosten genereren. De gemiddelde totale kosten in het jaar voorafgaand aan de behandeling zijn €11.126,-- per patiënt. De gemiddelde directe medische kosten zijn €7.398,-- per patiënt. Deze kosten bestaan met name uit kosten van klinische gezondheidszorg (33,1%) (bijvoorbeeld opnames in een algemeen of psychiatrisch ziekenhuis) en ambulante geestelijke gezondheidszorg (26,1%). De gemiddelde indirecte kosten zijn €3.728,-- per patiënt. Borderline- en obsessieve-compulsieve persoonlijkheidsstoornissen zijn significante voorspellers van hogere gemiddelde totale kosten. De economische ziektelast van onze patiëntenpopulatie was substantieel hoger dan de ziektelast gevonden in patiënten met depressie en gegeneraliseerde angststoornis, en vergelijkbaar met deze in patiënten met schizofrenie.

Wanneer de ziektelast in een patiëntenpopulatie hoog is, zal de maatschappij geneigd zijn meer te betalen voor het verkrijgen van gezondheidswinst (bijvoorbeeld een levensjaar).

De hierop volgende hoofdstukken beschrijven twee besliskundige modelstudies die de kosteneffectiviteit van verschillende vormen van psychotherapie vaststellen in de behandeling van cluster C persoonlijkheidsstoornissen (Hoofdstuk 4), bestaande uit de vermijdende, afhankelijke en obsessieve-compulsieve persoonlijkheidsstoornissen, en cluster B persoonlijkheidsstoornissen (Hoofdstuk 5), bestaande uit de borderline-, antisociale, theatrale en narcistische persoonlijkheidsstoornissen. We ontwikkelden een Markov cohortmodel waarin klinische en economische data van de SCEPTRE-trial zijn samengebracht om zo de behandelopties met elkaar te kunnen vergelijken in termen van kosten per hersteld patiënt jaar en kosten per voor kwaliteit gecorrigeerd levensjaar (quality-adjusted life year or QALY) over een periode van vijf jaar. Er zijn vier type parameters gebruikt in het model: (1) overgangskansen, (2) behandelkosten, (3) kosten van zorggebruik en productieverliezen gemaakt door patiënten en (4) utiliteiten van

de gezondheidstoestanden. Parameteronzekerheid werd onderzocht door het uitvoeren van een probabilistische analyse waarin distributies aan de parameters van het model werden toegekend. Resultaten indiceren dat, gebaseerd op de huidige beschikbare evidentie, er inderdaad kosteneffectieve behandelstrategieën beschikbaar zijn. Voor cluster C persoonlijkheidsstoornissen, liggen de punten waar de optimale behandeloptie verandert van kortdurend dagklinische psychotherapie naar kortdurend klinische psychotherapie bij een grenswaarde van €2.637,-- per hersteld patiënt jaar en €16.570,-- per QALY. Voor cluster B persoonlijkheidsstoornissen verandert de optimale behandeloptie van ambulante psychotherapie naar dagklinische psychotherapie naar klinische psychotherapie bij grenswaarden van €12.274,-- en €113.298,-- per hersteld patiënt jaar en €56.325,-- en €286.493,-- per QALY. De waargenomen ziektelast onder cluster B en cluster C persoonlijkheidsstoornissen geeft aan dat behandelingen tot €40.000,-- per QALY mogen kosten om acceptabel te zijn. Gebaseerd op deze kosteneffectiviteitsgrenswaarde, kan ambulante psychotherapie voor cluster B persoonlijkheidsstoornissen en kortdurend klinische psychotherapie voor cluster C persoonlijkheidsstoornissen worden aangemerkt als de meest kosteneffectieve keuze in termen van kosten per QALY.

Voortbordurend op deze kosteneffectiviteitsanalyses hebben we, in Hoofdstuk 6, de maximale opbrengst verkend van investeringen in verder onderzoek en implementatie-inspanningen. Zogeheten 'value of information' en 'value of implementation' analyses zijn uitgevoerd om de parameters te evalueren die het meeste bijdroegen aan de beslisonzekerheid van het model, en om de verwachte waarde van perfecte informatie (EVPI) en perfecte implementatie (EVPIM) te berekenen. Onze bevindingen geven aan dat de maatschappelijke waarde van verder onderzoek substantieel is en geschat wordt op €613 miljoen voor cluster B persoonlijkheidsstoornissen en €587 miljoen voor cluster C persoonlijkheidsstoornissen, uitgaande van een kosteneffectiviteitsgrenswaarde van €40.000,-- per QALY en het voortbestaan van psychotherapie voor nog ten minste vijf jaar. Meer bewijs omtrent behandelkosten en overgangskansen tussen gezondheidstoestanden is het meest waardevol. Door het huidige implementatieniveau van de kosteneffectieve behandelingen in de klinische praktijk in ogenschouw te nemen, blijkt er substantieel maatschappelijk voordeel in het veranderen van de capaciteit van en de therapietrouw aan de kosteneffectieve behandelstrategieën, met een geschatte EVPIM van €613 miljoen voor cluster B persoonlijkheidsstoornissen en €1.358 miljoen voor cluster C persoonlijkheidsstoornissen.

Vanuit het beleidsperspectief bevelen we daarom ambulante psychotherapie voor cluster B persoonlijkheidsstoornissen en kortdurend klinische psychotherapie voor cluster C persoonlijkheidsstoornissen aan, terwijl tegelijkertijd verder onderzoek naar en actieve implementatie van de kosteneffectieve behandelingen moet worden ondernomen voor een optimale toewijzing van het gezondheidszorgbudget.

Vooral in de huidige tijden van hervorming van de gezondheidszorg en economische crisis, wanneer de betaalbaarheid van de verzekeringsdekking onder de loep wordt genomen, neemt de bewustwording onder burgers toe dat de maatschappij grote zorg moet besteden aan het verstandig uitgeven van middelen. Meer studies zijn nodig die de kosten van gezondheidsinterventies, verder onderzoek en actieve implementatie afwegen tegen het maatschappelijke voordeel, vooral in de geestelijke gezondheidszorg. De afweging is simpel: wanneer we geld besparen door het behandelen van persoonlijkheidsstoornissen, het uitvoeren van verder onderzoek en het actief implementeren van kosteneffectieve behandelstrategieën, dan hebben we ons geld verstandig geïnvesteerd. Deze wijze van redeneren, traditioneel ver afstaand van de klinis-

che praktijk, is in toenemende mate realiteit aan het worden. De uitdaging wordt dus om deze nieuwe methoden en bevindingen van de besliskundige wetenschap te communiceren naar het grote publiek.

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Curriculum Vitae

Djøra Soeteman was born on March 16, 1978 in The Hague, the Netherlands. She graduated from the Dalton College in The Hague in 1996 and studied Veterinary Sciences at the University of Ghent in Belgium for two years. In 1998 she started Psychology at the University of Leiden from which she graduated with distinction in 2002 (Master's program in Clinical & Health Psychology). Her professional career began at the FORA institute in Leiden where she performed forensic psychological assessments in juvenile delinquents. She then got the opportunity to work as a researcher at the Viersprong Institute for Studies on Personality Disorders (VISPD) in Halsteren in 2003 and is since then as a PhD student connected to the Department of Medical Psychology and Psychotherapy of the Erasmus Medical Center in Rotterdam. In this position, she employed the cost-effectiveness part of the SCEPTRE-project as well as initiating several studies in juvenile crime prevention and intervention. Part of the research presented in this dissertation was performed under supervision of Dr. Jane Kim at the Center for Health Decision Science (CHDS) of the Harvard School of Public Health, where Djøra was so fortunate to pay a three-months work visit in 2008. The close collaboration that evolved caused her research focus to take definite shape in decision science applied to mental health care.

PhD portfolio

Name PhD student:	Djøra Soeteman
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1. PhD training

Relevant courses

2009 Systematic Review and Meta-Analysis of Direct, Indirect, and Mixed Treatment Evidence by Olivia Wu and Neil Hawkins, collaboration between Public Health and Health Policy, University of Glasgow and Oxford Outcomes

2008 Decision Analysis Methods in Public Health and Medicine by Jane J. Kim, Program in Health Decision Science, Department of Health Policy and Management, Harvard School of Public Health, Boston, MA, USA

2006 Advanced Modeling Methods for Economic Evaluation by Andrew Briggs, Mark Sculpher, Karl Claxton and Liz Fenwick, collaboration between the University of Glasgow and the Centre for Health Economics at the University of York

2006 A Cost-Effectiveness Modeling Methods Master course by Hans Severens, University of Maastricht

2006 Bayesian Approaches to Evidence Synthesis and Decision Modeling by Keith Abrams, University of Leicester

2003 Basics in Modeling in Economic Evaluation by Liz Fenwick, University of York

Presentations at national and international meetings

Decision Science Advanced Methods Seminar, Center for Health Decision Science, Harvard School of Public Health, Boston, December 2, 2009. Economic evaluation of psychotherapy for personality disorders: burden of disease, cost-effectiveness, and the value of further research and active implementation. Oral presentation.

31st Annual Meeting of the Society for Medical Decision Making, Hollywood (LA), October 18-21, 2009. Cost-effectiveness of psychotherapy for cluster C personality disorders and the value of further research and active implementation. Poster presentation.

XLV National Congress of Italian Psychiatry, Rome, October 11, 2009. Economic evaluation of psychotherapy for personality disorders: burden of disease and cost-effectiveness. Plenary presentation.

11th Conference of the International Society for the Study of Personality Disorders, New York City, August 21-23, 2009. Cost-effectiveness of psychotherapy for personality disorders. Oral presentation.

Lowlands Health Economists' Study Group (lolaHESG), Maastricht, May 28-29, 2009. Cost-effectiveness of psychotherapy for cluster C personality disorders. Paper discussion.

Annual Meeting of the Dutch Society of Psychotherapy. [Congres Nederlandse Vereniging voor Psychotherapie], Amsterdam, December 19, 2008. Cost-effectiveness of psychotherapy for personality disorders. [De kosteneffectiviteit van psychotherapie voor persoonlijkheidsstoornissen]. Plenary presentation.

35e Spring conference of the Dutch Society of Psychiatry. [35e Voorjaarscongres Nederlandse Vereniging voor Psychiatrie 'Psychiatrie in Europa'], Maastricht, April 11-13, 2007. The burden of disease in personality disorders: the first formal measurement of quality of life and societal costs. [De ziektelast van persoonlijkheidsstoornissen: een formele meting van kwaliteit van leven en maatschappelijke kosten]. Oral presentation.

8th Workshop on Costs and Assessment in Psychiatry: Investing in Mental Health Policy and Economics Research, ICMPE, Venice, March 9-11, 2007. The economic burden of personality disorders. Oral presentation.

Plenary Meeting of the EuroQol Group, Oslo, September 8-10, 2005. The EQ-5D used in mental health care: an unexpected sensitivity. Poster presentation.

iHEA 5th World congress, Barcelona, July 10-13, 2005. Burden of disease as moderator of cost-effectiveness arguments in psychotherapy: the YAVIS-argument. Poster presentation.

36th Annual Meeting of the Society for Psychotherapy Research, Montreal, June 22-25, 2005. Burden of disease in personality disorders: the societal costs and quality of life differentiated between disorders. Oral presentation.

7th Workshop on Costs and Assessment in Psychiatry, Venice, March 18-20, 2005. Burden of disease in personality disorders: the societal costs and quality of life differentiated between disorders. Oral presentation.

35th Annual Meeting of the Society for Psychotherapy Research, Rome, June 16, 2004. The burden of disease in psychotherapy patients with personality disorder. Oral presentation.

8th Conference of the International Society for the Study of Personality Disorders, Florence, October 9-12, 2003. The burden of disease in patients with personality disorder indicated for psychotherapy: Arguments for necessity of care. Oral presentation.

Grants

2008 Travel grant, 3-month work visit Harvard School of Public Health, Program in Health Decision Science, Department of Health Policy and Management (Trustfonds of the Erasmus University Rotterdam)

Publications in international scientific journals

Soeteman DI, Verheul R, Meerman AMMA, Rossum BV, Delimon J, Rijnierse P, Thunnissen M, Busschbach JJV, & Kim JJ (in press). Cost-effectiveness of psychotherapy for cluster C personality disorders. Journal of Clinical Psychiatry

Soeteman DI, Verheul R, Delimon J, Meerman AMMA, Eijnden E van den, Rossum BV, Ziegler U, Thunnissen M, Busschbach JJV, & Kim JJ (2010). Cost-effectiveness of psychotherapy for cluster B personality disorders. British Journal of Psychiatry, 196, 396-403

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Publications in national scientific journals

Boonstra C, Jonkman C, Soeteman DI, & Busschbach JJV (2009). Multisystemic treatment of serious antisocial and delinquent behaviour in youth: two year follow-up study. [Multi Systeem Therapie voor ernstig antisociale en delinquente jongeren: twee jaar follow-up studie]. Tijdschrift voor Systeemtherapie, 21, 94-105

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Book chapters

Soeteman DI, Hakkaart-van Roijen L, Busschbach JJV (2008). Cost-effectiveness. [Kosteneffectiviteit]. The Multidisciplinary Clinical Guideline for Treatment of Personality Disorders in The Netherlands (pp. 219-24). Utrecht: Trimbos-instituut.

Soeteman, DI, & Busschbach, JJV (2008). Cost-benefit and cost-effectiveness of prevention and treatment intervention. Accepted for publication in: R Loeber, W Slot, & P van der Laan (Eds). Tomorrow's Criminals: The Development of Antisocial Behaviour and Optimal Interventions.

Soeteman DI, & Busschbach JJV (2007). Health policy for psychotherapy: from subjective choices to economic models. [Beleidsvorming voor psychotherapie: van willekeur tot economische modellen]. In: R Verheul & JH Kamphuis (Eds). De toekomst van persoonlijkheidsstoornissen (pp.189-200). Houten/Diegem: Bohn Stafleu Van Loghum.

2. Teaching

Fall 2009	Head teaching assistant, Course: Decision Analysis for Health and Medical Practices, Lectured by Prof. Dr. Sue Goldie, Department of Health Policy and Management and the Department of Biostatistics, Harvard School of Public Health, Boston, MA, USA
2002-2003	Lecturer, Department of Clinical and Health Psychology, University of Leiden
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