Economic evaluation in mental healthcare
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Chapter 1

Introduction
Mental disorders are currently acknowledged to be among the most disabling illnesses worldwide. The proportion of the population that will be directly affected by at least one form of mental illness is disturbingly high; lifetime prevalence estimates range from 25% to 41% for Western countries (1, 2). Moreover, it has been indicated that the burden of mental illness will even increase in coming decades (3). Persons with mental illness may present a wide variety of signs and symptoms, and there are large differences between disorders in terms of subjective well-being and impairments experienced in daily functioning. Major depressive disorder and schizophrenia are generally regarded as two of the most disabling forms of mental illness (4, 5). The studies combined in this thesis focus on economic aspects of interventions in patient populations with these disorders.

Main symptoms of **major depressive disorder** include a depressed mood and general loss of interest (6), regularly accompanied by additional symptoms like sleep disturbances, concentration problems, and suicidal ideation or suicide attempts. Depression is associated with high lifetime prevalence rates, estimated at 15% (2), and often runs an intermittent lifelong course with multiple relapses and recurrences (7). Most patients are treated in primary care, where treatment consists of antidepressants and psycho-education. However, management of depression by general practitioners seems to be less than optimal considering the high rate of recurrences and related negative long term consequences (8). An additional complicating aspect for the treatment of depression concerns the limited number of available therapists in secondary care. Consequently, many patients with depression (often with comorbid anxiety disorders) do not receive adequate treatment (9).

**Schizophrenia** (and related psychotic disorders) is considered to be a complex mental illness that negatively affects fundamental aspects of human functioning. The disorder can be characterised by positive symptoms, including distortions in thinking and perception, and negative symptoms like affective flattening and poverty of speech (6). Estimated prevalence rates range from 0.5% to 0.7% (10). After a first episode of psychosis, guidelines generally recommend the continuation of antipsychotic drugs for at least one to two years following remission. This approach is often successful in preventing relapses, but may also lead to disabling side effects and low compliance. Besides psychopharmacological treatment, care as usual for schizophrenia in the Netherlands consists of psycho-education, support of the patients and their relatives, and individual therapy. Despite the availability of these various treatment options, the majority of patients with schizophrenia continue to have disabling residual symptoms, including persistent auditory hallucinations, and remain handicapped in social functioning.
In addition to the considerable impact of mental illness on the lives of patients, the economic consequences for society are substantial as well. It has been estimated that 1% to 2% of healthcare expenses in Western countries is spent on the treatment of depressive disorders (11, 12), while costs of schizophrenia account for 1% to 3% (11, 13). The extensive use of healthcare resources of patients with depression or schizophrenia is related to the early age at onset in combination with the often chronic (intermittent) course of both disorders (14, 15, 16). The potential financial consequences for society become even more apparent when including costs outside the healthcare sector, like costs of informal care or productivity losses that can be particularly high, especially for patients with depression (12).

In previous decades, decision-makers gradually seem to have become aware of the high disability related to mental illness and the rising costs of mental healthcare. This has resulted in a growing demand for information on both costs and health outcomes to prioritise between alternative interventions and to support reimbursement decisions. However, only few economic evaluations had adequately examined interventions in the area of mental healthcare in the mid 1990s. For most countries and healthcare systems, information on economic aspects was scarce or even absent (17, 18).

Most of the studies available at that time had focused on clinical and economic aspects of psychopharmacological treatment, both in patients with depression (19) and schizophrenia (20, 13). Unfortunately, interpretation of studies on psychopharmacological treatment was generally hampered by short follow-up periods, small numbers of included patients, high drop-out rates, and a narrow scope of included costs. Several economic evaluations had examined psychosocial interventions aimed at depression. Since patients with depression are mainly treated in primary care, studies often compared costs and health outcomes of treatment by general practitioners with outcomes of alternative interventions like cognitive therapy or case management (21, 22). However, clear differences in costs and health outcomes between these interventions and care as usual provided by general practitioners could generally not be found. Detailed economic studies focusing on psychosocial interventions for schizophrenia were scarce, and available results appeared to be inconclusive (23, 24). However, there were indications that interventions like cognitive therapy or behavioural family treatment had the potential to be cost-effective in patients with schizophrenia (25, 26).

In the Netherlands, the importance of economic studies in the area of mental healthcare, and the sheer absence of such studies in the Dutch healthcare system, was recognised in the late 1990s. At that time, the Dutch Ministry of Health, Welfare and Sport had already been stimulating economic evaluations in various
other areas of healthcare. The acknowledged importance of economic studies in mental healthcare resulted in the prioritisation of research on this topic. In the following years, various economic evaluations in mental healthcare were funded by the Dutch National Health Insurance Board (currently CVZ) and ZonMw (Netherlands Organisation for Health Research and Development), including the studies combined in this thesis.

Economic evaluation: a brief overview

Due to scarcity of resources, priorities have to be set for programmes and interventions in all areas of healthcare. Economic evaluation is an important tool to provide information on costs and health outcomes of alternative interventions to decision-makers, and is considered to be essential for rational priority decisions (27).

Most economic evaluations conducted in the area of mental healthcare were designed as cost-effectiveness studies (24, 17). In cost-effectiveness analysis, costs and health outcomes associated with an intervention are used to calculate the incremental cost-effectiveness ratio relative to one or more alternatives (28). Cost-effectiveness studies are generally conducted alongside randomised clinical trials, often comparing newly developed treatment approaches with standard treatment or regular care as provided in the patient population under study. Health outcomes included in cost-effectiveness analysis in mental healthcare are commonly based on disease-specific instruments, instead of generic (preference-based) outcome measures generally recommended by guidelines. For decision-makers, comparisons across disorders or studies are complicated when disease-specific instruments are applied. Since cost-effectiveness analysis requires health outcomes to be expressed in a single (overall) score, some reliable and valid questionnaires that only provide scores on subscales or domains cannot directly be applied in this type of economic evaluation.

In order to assess all the relevant consequences of interventions under study, economic evaluations are preferably conducted from a societal perspective (29). When applying a societal perspective, both medical costs and costs outside the healthcare sector are part of the analysis. Information on the use of healthcare services and other cost aspects is often collected by means of questionnaires (repeatedly) administered to the patients included in a study. Costs are subsequently calculated by multiplying registered quantities with cost prices. In the Netherlands, standard cost prices for frequently used types of costs have been combined in a cost manual, aiming to improve the comparability of studies (30). However, for various services provided in mental healthcare, standard cost prices
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are currently unavailable and true costs of resource use have to be estimated in the context of a specific study. The skewed distribution of costs may lead to methodological and interpretational difficulties, not only in case of analysing cost data, but also when presenting results to decision-makers. Although medians may better represent central tendency in skewed distributions, information on mean costs (and differences in mean costs) is most relevant for decision-makers (31). Nowadays, the bootstrap method (32) is regularly applied to provide information about the uncertainty of economic results. Bootstrap analyses can be used, among other things, to assess confidence intervals surrounding differences in mean costs between groups. Missing cost data may cause difficulties for economic analyses, especially when missingness appears to be not completely at random (33). Since drop-out of patients can be substantial in mental healthcare, it is important to be aware of the potential bias related to incomplete patient data. There are currently various techniques available to handle missing data in economic studies (34).

Aim and overview of the thesis

The main objective of the studies combined in this thesis was to assess the cost-effectiveness of various interventions for patients with mental illness in the context of the Dutch healthcare system. These interventions were primarily aimed at major depressive disorder and schizophrenia, disorders that are associated with serious impairments for patients and considerable costs for society.

Chapter 2 presents the results of an economic evaluation examining Hallucination focused Integrative Treatment (HIT) in patients with schizophrenia and persistent auditory hallucinations. The HIT programme combines cognitive behaviour therapy with various other treatment modalities, including neuroleptics, coping training, and single family treatment. In previous studies, HIT appeared to be effective in reducing signs and symptoms in various patient populations with auditory hallucinations. The intervention was expected to lead to less intensive healthcare utilisation and lower associated costs, but economic aspects of HIT had not been studied in detail before.

Chapter 3 describes a cost-effectiveness study comparing Cognitive Self-Therapy (CST) with treatment as usual in patients with depression and comorbid anxiety disorders. Previous studies had indicated that self-help interventions can be effective in patients with mental illness. CST is a method that aims to restructure cognitive schemata and address problems in social functioning and relationships. After successfully completing various training phases, patients are allowed to attend CST sessions led by peers. The potential cost savings associated with self-
help interventions like CST seemed particularly relevant for policy makers, but economic studies had rarely been conducted. 

Chapter 4 describes the findings of an economic study focusing on a Psycho-Educational Prevention programme (PEP) aimed at primary care patients with depression. Depression is associated with a high risk of recurrence, which not only has negative consequences for patients involved but also leads to considerable healthcare costs. PEP consists of contacts between patients and prevention specialists, educational meetings on depression management, and telephone monitoring. Two enhancements of PEP, i.e. additional psychiatric consultation and cognitive behavioural therapy sessions, were also compared to care as usual provided by general practitioners. In order to register relevant long term outcomes, patients were prospectively followed for three years. This study was the first to examine economic aspects of PEP in a European healthcare setting. 

The purpose of the study presented in Chapter 5 was to examine differences in costs and health outcomes related to alternative medication approaches in patients with first onset psychosis. Guidelines generally recommend maintenance treatment in this patient population, which is successful in preventing relapses but also associated with disabling side effects. Alternatively, guided discontinuation strategy could be applied, in which the use of antipsychotics is gradually decreased, and eventually completely discontinued if possible. This second approach seems less intrusive for patients, but may lead to more relapses. Information on both costs and health outcomes of these medication strategies in patients with first-episode psychosis was required to support policy decisions. 

In contrast to most guidelines and recommendations, economic evaluations in mental healthcare are often designed as cost-effectiveness studies that include primary outcome measures aimed at a specific aspect of health. Chapter 6 presents the difficulties and potentially negative consequences related to the selection of single outcome measures for cost-effectiveness studies in mental healthcare. The various aspects of this topic are illustrated by alternative analyses based on data collected during the HIT study.

Finally, Chapter 7 discusses the overall findings of the previous chapters, and will provide recommendations for future economic evaluations and related research in the area of mental healthcare.
References


