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

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A B S T R A C T

Objective: 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. The objective of this study was to assess the societal value of conducting further research to inform reimbursement decisions and implementation of cost-effective psychotherapy for clusters B and C personality disorders (PDs).
Methods: Value of information and value of implementation analyses were conducted using previously developed cost-effectiveness models for clusters B and C PDs 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 €425 million for cluster B PDs and €315 million for cluster C PDs, 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 transition probabilities and health state costs. The pEVPIM was estimated to be €595 million for cluster B PDs and €1,372 million for cluster C PDs, suggesting that investing in implementation of cost-effective psychotherapy is likely to be worthwhile.
Conclusions: The societal value of additional research on psychotherapy for clusters B and C PDs is substantial, especially when prioritizing information on transition probabilities and health state costs. Active implementation of cost-effective treatment strategies into clinical practice is likely to improve the efficiency of health care provision in The Netherlands.

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Introduction

Cost-effectiveness analyses increasingly are 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 (PDs) [1], including borderline, antisocial, histrionic, and narcissistic PDs, and cluster C PDs [2], including avoidant, dependent, and obsessive-compulsive PDs. Results indicate that, at a societal willingness to pay of €40,000 per quality-adjusted life year (QALY), outpatient psychotherapy is the optimal treatment for patients with cluster B PDs, whereas short-term inpatient psychotherapy is the most cost-effective choice for patients with cluster C PDs. 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 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 because it is expected to reduce decision uncertainty and, thus, the probability and the net consequences of a wrong decision; however, it 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 places an upper bound on the value of conducting further research regarding the decision question of cost-effective psychotherapy for clusters B and C PDs and aims to feed the priority-setting process by indicating 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 empirical data

Based on the prevalence of cluster C PDs (median 4.2%; 1.4% avoidant PDs, 0.8% dependent PDs, and 2.0% obsessive-compulsive PDs) [8] in the population of The Netherlands (16,377,153), the percentage of treatment-seeking patients with a PD (19.1%) [9], and the percentage of patients with a PD receiving psychotherapy (16.4%), we estimated the annual incident cluster C PD population eligible for treatment to be 21,546 patients. The total eligible population (discounted over 5 years) was calculated to be 99,756. The various modalities of psychotherapy in treating patients with cluster C PDs include long-term outpatient psychotherapy, short-term and long-term day hospital psychotherapy, and short-term and long-term inpatient psychotherapy.

For cluster B PDs (median 6.0%; 1.5% borderline PDs, 2.6% antisocial PDs, 1.8% histrionic PDs , and 0.1% narcissistic PDs) [8], we assumed the incidence of eligible patients per annum to be 30,780 and the total eligible population (discounted over 5 years) to be 142,508. Treatment options include outpatient psychotherapy, day hospital psychotherapy, and inpatient psychotherapy.

Patient-level data were obtained from the largest existing clinical trial of psychotherapy for PDs (the SCEPTRE trial), which included over 900 patients [1,2]. Patients were assigned to one of the treatment groups, based on a comprehensive assessment battery combined with the expert opinion of clinicians. To avoid selection bias, we controlled for initial differences in patient characteristics with the multiple propensity score method [10].

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. For long-term outpatient psychotherapy, short-term day hospital psychotherapy, long-term day hospital psychotherapy, and long-term inpatient psychotherapy, we estimated the current level of implementation to be 0.214, 0.190, 0.230, and 0.225, respectively. For cluster B PDs, 57 out of 241 patients received outpatient psychotherapy; therefore, we assumed the current level of implementation to be 0.237. For day hospital psychotherapy and inpatient psychotherapy the current level of implementation was estimated to be 0.411 and 0.353, respectively.

Cost-effectiveness analysis and decision uncertainty

Cost-effectiveness analyses were previously conducted using a Markov cohort model based on second-order Monte Carlo simulation [11]. Results were reported from the societal perspective and in terms of costs per QALY gained. To be consistent with most other cost-effectiveness studies that are based on clinical

Table 1 – Cost-effectiveness results over five years [1,2].

Psychotherapy dosage	Cluster C PD			
	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
Modality of psychotherapy	**Cluster B PD**			
	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.

trials in the literature, we selected a five-year time horizon, which is two years beyond the duration of the clinical trial.

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 the SCEPTRE trial. Each parameter was assigned a distribution of values in order to characterize the uncertainty in the data (e.g., gamma distributions for costs, beta distributions for utilities). We assumed probability parameters followed a Dirichlet distribution, a continuous distribution that is the multivariate generalization of the beta distribution. 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. The expected costs, and expected QALYs for each treatment strategy were calculated 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) [12], 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 willingness-to-pay threshold values. As reported previously, we found that outpatient psychotherapy was the most cost-effective treatment for cluster B PDs and short-term inpatient psychotherapy for cluster C PDs at a threshold of €40,000 per QALY (Table 1).

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 2). 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 PDs, perfect information would eliminate the possibility of making the wrong reimbursement decision. The expected values of perfect information (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 EVPI was calculated, illustrated in Table 3 for a cluster C patient. The table represents output from 6 of the total 1000 simulations generating net monetary benefits for each of the treatment strategies. With current information, short-term inpatient psychotherapy is the optimal decision because this intervention generates the highest expected net benefit (€51,124, at a threshold of €40,000 per QALY). With perfect information the decision

Table 2 – Framework matrix for determining the expected value of perfect information and of perfect implementation [6].

	Information	
	Current	Perfect
Implementation		
Current	A	B
Perfect	C	D

Table 3 – Calculating expected value of perfect information (EVPI) for an individual cluster C patient.

Simulation		Net monetary benefits*					Maximum net benefit	Benefits forgone
		Long-term outpatient	Short-term day hospital	Long-term day hospital	Short-term inpatient	Long-term inpatient		
	Expectation	€42,135	€48,001	€33,670	€51,124	€19,731	€54,283	€3,159
1		<u>€55,335</u>	€49,862	€30,609	€53,739	€47,329	€55,335	€1,595
2		€38,142	€42,243	€29,939	<u>€52,331</u>	€32,884	€52,331	€0
3		€49,584	<u>€53,749</u>	€26,813	€49,132	€48,165	€53,749	€4,617
4		€55,344	€51,292	€46,785	<u>€62,637</u>	€48,807	€62,637	€0
5		€41,341	<u>€55,000</u>	€36,338	€48,924	€7,029	€55,000	€6,075
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1000		€48,833	€47,462	€34,071	<u>€68,596</u>	€7,354	€68,596	€0

Decision based on current information: Short-term inpatient psychotherapy.
Decision based on perfect information: underlined.
Expected net benefit with current information: €51,124.
Expected net benefit with perfect information: €54,283.
Expected value of perfect information: €54,283 − €51,124 = €3,159.
* Net monetary benefit was calculated by multiplying effect by societal willingness to pay and subtracting cost, with willingness to pay set at a ratio of €40,000 per QALY.

maker could choose the alternative with the maximum net benefit for each simulation; that is, choose long-term outpatient psychotherapy for simulation 1. short-term inpatient psychotherapy for simulation 2, short-term day hospital for simulation 3, and so on. The benefits forgone are the difference in the net monetary benefits between the optimal strategy for a given simulation and the strategy identified as optimal in the adoption decision (i.e., short-term inpatient psychotherapy). The expectation of benefits forgone over all simulations represents the EVPI per individual (€3,159, at a threshold of €40,000 per QALY). This result can also be calculated by taking the difference between the expected net benefit with perfect information (cell D in Table 2) and the expected net benefit with current information (cell C in Table 2).

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 2) and the expected net benefit with implementation at its current level (cell A in Table 2). 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 2) and the expected net benefit with information and implementation at its current level (cell A in Table 2).

We assumed the expected lifetime of psychotherapy (i.e., the time horizon over which additional research would be useful) to be five years, but explored the influence of a longer time horizon.

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 [13].

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 five years.

Table 4 – Framework matrix for different dosages of psychotherapy in treating cluster C personality disorders.

For individual patients (€)

	Information	
	Current	Perfect
Implementation		
Current	37,370 (A)	37,370 (B)*
Perfect	51,124 (C)	54,283 (D)

For the total eligible population (€ millions)

	Information	
	Current	Perfect
Implementation		
Current	3,728 (E)	3,728 (F)*
Perfect	5,100 (G)	5,415 (H)

Societal willingness to pay per QALY €40,000
Total eligible population over 5 years 99,756
EVPI for patient = D − C = €3,159
pEVPI (in million) = H − G = €315
EVPIM for patient = C − A = €13,754
pEVPIM (in million) = G − E = €1,372
EVP for patient = D − A = €16,913
pEVP (in million) = H − E = €1,687

EVP, expected value of perfection; EVPI, expected value of perfect information; EVPIM, expected value of perfect implementation; pEVP, EVP of the population; pEVPI, EVPI of the population; pEVPIM, EVPIM of the population.

* Given the simplifying assumption that the level of implementation is not influenced by the level of information, the expected value of the decision made on the basis of perfect information (cell B) was equivalent to the expected value of the decision made on the basis of current information (cell A).

In sensitivity analyses, the decision uncertainty and population EVPI, EVPIM, and EVP were calculated for different values of the willingness-to-pay threshold. In addition, we studied the impact of the current level of implementation, the time horizon of analysis, 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 1,000 Monte Carlo simulations with 1,000 draws from the parameter group of interest.

Results

Base case analysis

Table 1 summarizes the currently available evidence on the costs and effects of the five alternative treatment dosages of psychotherapy for cluster C PDs and three psychotherapy modalities for cluster B PDs, 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 PDs 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; therefore, there is value in reducing the error probability of 0.48 by collecting additional evidence. Assuming implementation is perfect, the EVPI for individual patients is €3,159 over a five-year time horizon; with 99,756 eligible patients in the population, the pEVPI is €315 million (Table 4). Based on the current level of information, the EVPIM for individual patients is €13,754 over a five-year time horizon; with 99,756 eligible patients in the population, the pEVPIM) is €1,372 million.

Likewise, outpatient psychotherapy provides the highest expected net benefit for cluster B PDs (€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 EVPI for individual patients is €2,984 over a five-year time horizon and the pEVPI is €425 million (Table 5).

Based on the current level of information, the EVPIM for individual patients is €4179 over a five-year time horizon and €595 million for the eligible population (pEVPIM).

The population expected value of perfection (pEVP) was €1,687 million for cluster C PDs (€16,913 for individual patients) (Table 4) and €1,021 million for cluster B PDs (€7,163 for individual patients) (Table 5), suggesting that there is considerable scope for improving the efficiency of health care provision for cluster B and cluster C patients with PDs.

Figure 1A displays the 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 transition probabilities and health state costs are relatively high; research that would eliminate the uncertainty in these subsets of parameters would be worth €232 million and €39 million, respectively (€2328 and €390 for individual patients). In contrast, the model input parameters related to

Table 5 – Framework matrix for different modalities of psychotherapy in treating cluster B personality disorders.

For individual patients (€)

	Information	
	Current	Perfect
Implementation		
Current	39,893 (A)	39,893 (B)*
Perfect	44,072 (C)	47,056 (D)

For the total eligible population (€ millions)

	Information	
	Current	Perfect
Implementation		
Current	5,686 (E)	5,686 (F)*
Perfect	6,281 (G)	6,706 (H)

Societal willingness to pay per QALY €40,000
Total eligible population over 5 years 142,508
EVPI for patient = D − C = €2,984
pEVPI (in million) = H − G = €425
EVPIM for patient = C − A = €4,179
pEVPIM (in million) = G − E = €595
EVP for patient = D − A = €7,163
pEVP (in million) = H − E = €1,021

EVP, expected value of perfection; EVPI, expected value of perfect information; EVPIM, expected value of perfect implementation; pEVP, EVP of the population; pEVPI, EVPI of the population; pEVPIM, EVPIM of the population.

* Given the simplifying assumption that the level of implementation is not influenced by the level of information, the expected value of the decision made on the basis of perfect information (cell B) was equivalent to the expected value of the decision made on the basis of current information (cell A).

treatment costs have lower value of information (€1.4 million or €14 for individual patients), and health state utilities have hardly any value of information (€162,759 or €2 for individual patients). Note 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.

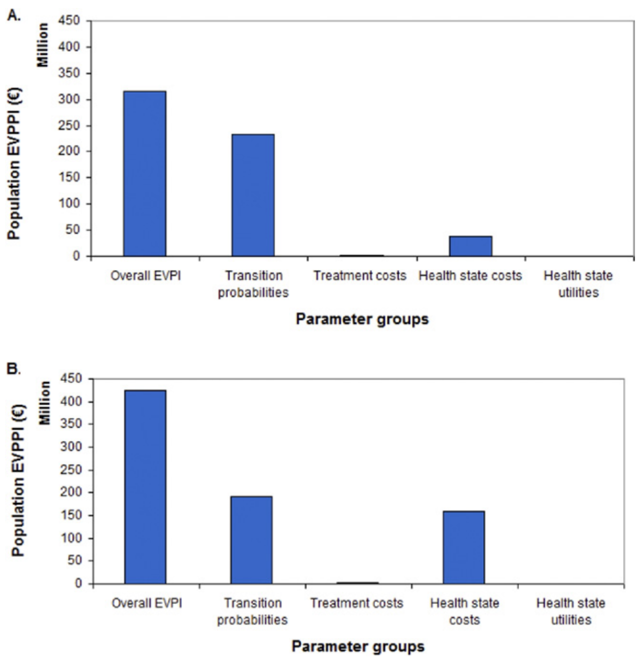


Fig. 1 – Population expected value of partial perfect information (pEVPPI) at a cost-effectiveness threshold of €40,000 per QALY and assuming a 5-year lifetime for psychotherapy. A, pEVPPI for cluster C PDs. B, pEVPPI for cluster B PDs.

Figure 1B shows that the pattern of partial EVPI for cluster B PDs is very similar to that of cluster C PDs, with relatively high values associated with transition probabilities and health state costs (pEVPPI of €193 million and €160 million, respectively; €1351 and €1123 for individual patients). The value of information associated with treatment costs is much lower (€1.4 million; €10 for individual patients), and the value associated with health state utilities is zero.

Sensitivity analysis

Level of the societal willingness to pay per QALY

Figure 2A 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 PDs. 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 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

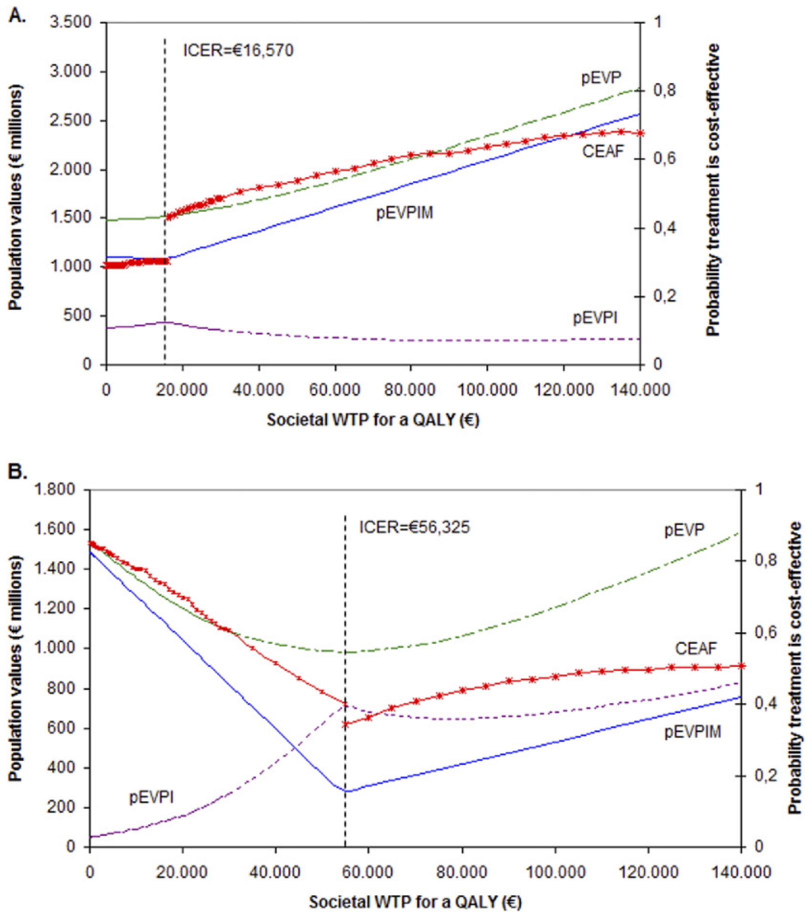


Fig. 2 – Population expected values of perfect information (pEVPI), perfect implementation (pEVPIM), and perfection (pEVP) (primary axis) and cost-effectiveness acceptability frontier (CEAF) (secondary axis) as a function of the societal willingness to pay (WTP) for the adoption decision regarding(A) the five treatment strategies for cluster C PDs and (B) the three treatment strategies for cluster B PDs.

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 (e.g., 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.

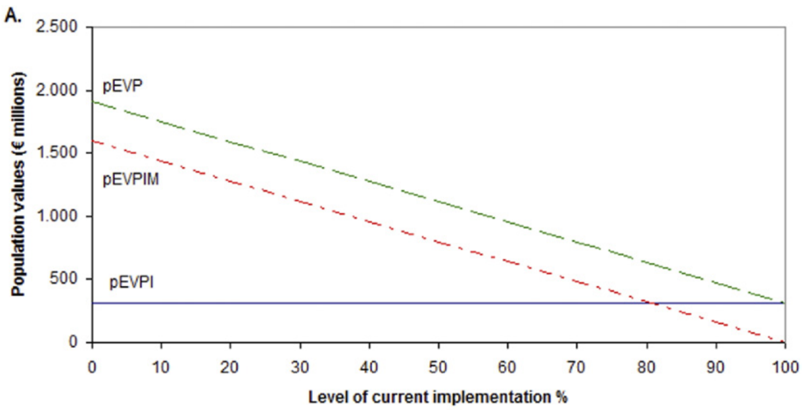
The pEVP curve can be derived by summing pEVPI and pEVPIM and displays a gradual increase over the full range of threshold values.

Figure 2B 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 PDs. 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 3 displays the impact of the level of current implementation on the expected population values of information



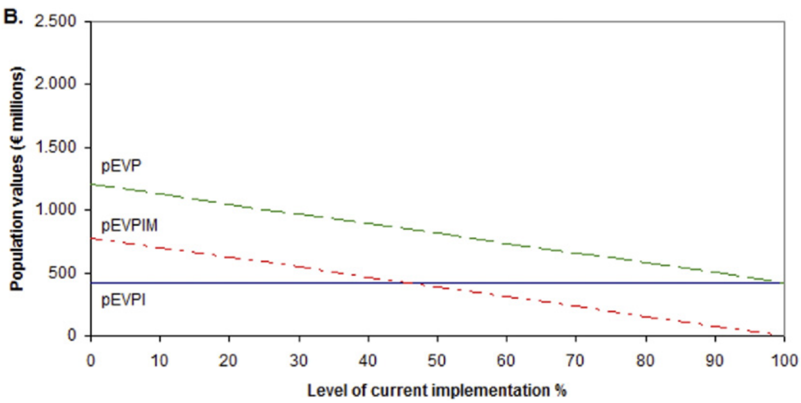


Fig. 3 – Population expected values of perfect information (pEVPI), perfect implementation (pEVPIM), and perfection (pEVP) as a function of the level of current implementation of the most cost-effective treatment at a threshold of €40,000 per QALY. A, short-term inpatient psychotherapy for cluster C PDs. B, outpatient psychotherapy for cluster B PDs.

(pEVPI), implementation (pEVPIM), and perfection (pEVP). At a cost-effectiveness threshold of €40,000 per QALY, outpatient psychotherapy for cluster B PDs and short-term inpatient psychotherapy for cluster C PDs 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 €1,597 million for cluster C PDs (Fig. 3A) and €780 million for cluster B PDs(Fig. 3B). With an increasing level of current implementation, the pEVPIM curve decreases as more patients 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.

Selection of time horizon

Varying the time horizon over which the pEVPI, pEVPIM, and pEVP are calculated influenced the results crucially (Fig. 4). We found that as we extended the time horizon beyond five years, the population expected values increased.

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.

Discussion

Extending from previous cost-effectiveness analyses, we estimated the societal value of conducting additional research related to the adoption decisions of cost-effective psychotherapy for cluster B and cluster C PDs. 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. Simultaneously, 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 €425 million for cluster B PDs and €315 million for cluster C PDs, assuming a willing-

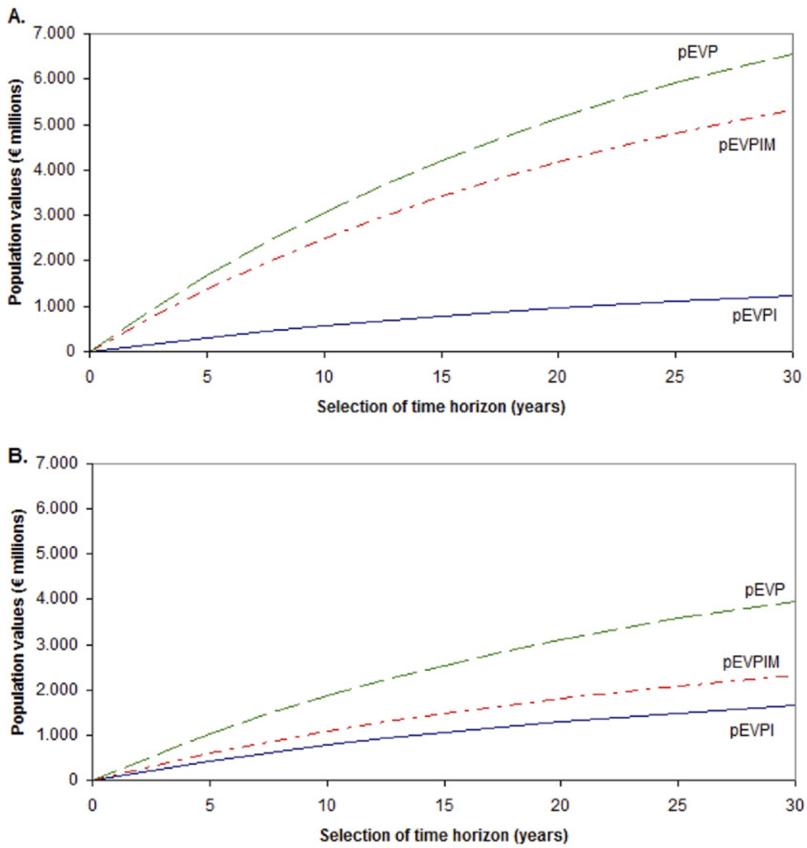


Fig. 4 – Population expected values of perfect information (pEVPI), perfect implementation (pEVPIM), and perfection (pEVP) as a function of the selection of time horizon at a threshold of €40,000 per QALY. A, short-term inpatient psychotherapy for cluster C PDs. B, outpatient psychotherapy for cluster B PDs.

ness-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 transition probabilities between health states and health state costs would be most valuable, whereas additional evidence about treatment costs and health state utilities would be of relatively little or no value. Considering the current level of implementation of cost-effective psychotherapy 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 EVPIM estimated to be €595 million for cluster B PDs and €1,372 million for cluster C PDs.

The upper bound 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) [14].

The EVPI and EVPIM provide the necessary, but not sufficient, conditions for further research and implementation; whether these activities should be undertaken requires knowledge of the expected net benefit from a particular research or implementation project (i.e., the difference between the expected value of sample information and the cost of specific research). It is important to emphasize that only when a future study has a probability of changing the optimal strategy will there be benefits in terms of a reduction in the expected loss from uncertainty. In formulating policy recommendations and prioritizing research and/or implementation, the expected net benefit from a particular research or implementation project regarding psychotherapy for clusters B and C PDs should be compared with the expected net benefit of other unrelated proposed clinical research and implementation projects. From the policy perspective, we recommend reimbursement of outpatient psychotherapy for cluster B PDs and short-term inpatient psychotherapy for cluster C PDs while simultaneously commissioning further research into the cost-effectiveness of proposed clinical research and implementation projects in order to more efficiently allocate health care resources.

In our expected value of information calculations, we arbitrarily selected a time horizon of five years, commonly used in clinical trial-based cost-effectiveness analyses. Although it has been suggested that the analytic time horizon should ideally encompass future changes in technologies, prices, and evidence, there are currently no well-established methods in choosing the appropriate time horizon [15].

The pEVPI, pEVPIM, and pEVP are heavily influenced by the level of current implementation, the size of the eligible patient population, the selected time horizon, and the societal willingness to pay per QALY. Depending on these factors, policy recommendations between technologies can differ substantially, and results should be considered in light of the assumptions made by the researchers.

Although the EVPI analyses suggest that further research may be justified to support the future adoption decisions of cost-effective psychotherapy for cluster B and cluster C PDs, the partial EVPI analyses for the four groups of parameters indicate that this may not require an experimental design. More precise estimates of health state costs, for example, which account for 45% (cluster B model) and 14% (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 patients with PDs. Thus, although additional evidence about transition probabilities is valuable, gathering information on 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.

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 [16–18]. 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 PDs is 0.237, and for short-term inpatient psychotherapy for cluster C PDs 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 patients with PDs 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 patients, percentage of patients receiving psychotherapy) is not available for The Netherlands; therefore, we relied on data from other settings. Furthermore, our calculations were based on the simplifying 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. The framework could be adapted to incorporate this relationship. Finally, as discussed earlier, inherent to the assessment of the EVPI and the EVPIM, information is rarely perfect. Therefore, the framework could be extended in order to calculate the expected value of sample information (EVSI) and the expected value of specific implementation (EVSIM), indicating the societal value of information from specific research or of specific implementation strategies.

Despite these limitations, our findings suggest that the societal value of additional research on treatments for clusters B and C PDs is substantial, particularly when prioritizing information on transition probabilities and health state costs. 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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