Cost-effectiveness of preventing depressive recurrences by psychological interventions; a population health economic modelling study

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Chapter 4

ABSTRACT

Introduction Largely owing to its recurrent nature, major depressive disorder (MDD) is associated with high economic costs.

Aim Our aim was to investigate whether offering preventive psychotherapies would improve the cost-effectiveness of the Dutch health care system for recurrent MDD.

Method A health economic model was used to assess return on investments (ROI). We compared a base-case scenario (enhanced TAU) with four scenarios in terms of cost-effectiveness: enhanced TAU plus A) cognitive therapy, CT; B) mindfulness-based CT, MCT; C) interpersonal therapy, IPT and D) a hypothetical ‘supported self-help’ based on preventive CT.

Results The ROI of enhanced TAU is €1.30 (£1.10) while the ROI of adding IPT, CT or MCT is €1.31 (£1.10), €1.43 (£1.21) and €1.45 (£1.22) respectively. In order to reach the most competitive ROI (€1.45), the supported self-help needs to reach a relative risk reduction of 0.71.

Discussion Adding CT, MCT or a supported self-help might make the healthcare system for recurrent MDD more cost-effective compared to enhanced TAU only.

Implications for practice Due to an unsustainable expenditure for mental health, governments are forced to allocate resources to interventions that maximise cost-effectiveness. This study shows cost-effective alternatives for the continuation of medication in recurrently depressed patients.
INTRODUCTION

Major depressive disorder (MDD) affects 16% of the population on a lifetime basis\(^1\) and is associated with a high risk of relapse\(^2\). Of all people with MDD, at least 80% experience recurrent depressive disorder\(^1\) with five\(^1\) to nine\(^3\) depressive episodes over the course of their life and spend as much as 21% of their lifetime in a depressed condition\(^6\). In the specialised mental health care, the percentage of recurrence is even higher, up to 85% over 15 years\(^7\). MDD is therefore perhaps best described as a largely chronically recurrent disorder with much of its disease burden stemming from its recurrent nature. Partly due to its recurrent nature, MDD has substantial economic consequences\(^8\)–\(^11\). Reducing the disease burden of depressive disorders by preventing new episodes at affordable costs is therefore of great public health significance.

A recent meta-analysis by Biesheuvel et al\(^12\) showed that preventive psychological interventions were significantly better in reducing the risk of relapse or recurrence when compared to treatment-as-usual (TAU) (RR=0.64, 95%CI:0.53-0.76, \(z=4.89\), \(p<0.001\), NNT=5) and even when compared to anti-depressant medication (ADM) (RR=0.83, 95%CI:0.70-0.97, \(z=2.40\), \(p=0.017\), NNT=13).

Though clinical evidence is promising, due to the mounting pressure on healthcare budgets, there is an additional need to also incorporate economic evidence to guide healthcare policies. To be able to assess the cost-effectiveness of (multiple) interventions, Lokkerbol et al\(^13\) developed a health economic (Markov) model that synthesizes clinical, economic and epidemiological evidence. In the model, we used a base-case scenario (enhanced TAU) and compared this with enhanced TAU plus various psychological interventions to prevent recurrence in depression.

In our study we used this Markov model to answer the following research questions:

1. Do preventive psychological interventions for recurrences in depressive disorder improve the cost-effectiveness over and above enhanced TAU?
2. What preventive psychological intervention makes the largest contribution in improving the health care system's cost-effectiveness?

Since the available interventions often rely on intensive use of therapist's time and are therefore costly, we asked ourselves if there would be room for a (hypothetical) low-cost supported self-help intervention. Therefore, we will also use the Markov model to answer following research question:

3. How effective needs a hypothetical low-cost supported self-help intervention be to become competitive in terms of its cost-effectiveness relative to CT, MCT and IPT?
METHODS

Cost-effectiveness at health care system level
An easy indicator to describe the ratio between effectiveness and intervention costs at population level is the return on investment (ROI). The ROI is computed as (DALYs averted * WtP) / (costs enhanced TAU + (per-patient preventive intervention costs * number of patients)). DALY stands for reduction of disability-adjusted life-years, i.e. the reduction of the number of years lost due to disability and due to premature death. In this study we use the lower WtP bound of €20,000 (£16,859) for one DALY averted. Both benefits and costs are expressed in € (£). A higher ROI for an added intervention is more favourable. This indicator helps to make quick and easy comparisons across competing interventions.

Enhanced TAU
The enhanced TAU scenario, which forms the basis for the comparisons, is an evidence-based healthcare system for depressive disorder in full agreement with the Dutch clinical guidelines for the treatment of depression, which is quite similar to the well-accepted NICE guidelines. The enhanced TAU scenario is not only “evidence-based” (guideline congruent), but also “preference-based” in the sense that interventions were endorsed by both patients and health care professionals (see Lokkerbol et al 13 for a full description).

Preventive psychological interventions
According to the literature, various interventions in the continuation or maintenance phase are available for the prevention of recurrent depressive disorder (Biesheuvel-Leliefeld et al. 2014). In our study, the reviewed interventions were preventive cognitive therapy (CT), mindfulness-based cognitive therapy (MCT) and interpersonal therapy (IPT). CT is based on Beck's theory that negative automatic thoughts, maladaptive information processing, and avoidance behaviour play a key role in the development and maintenance of depression 14. MCT is a protocol-led, group-based skills training program designed to teach remitted patients how to disengage from automatic, cognitive processing patterns linked to depressive relapse 15. IPT originates from interpersonal theory 16. It links stressful life events and insufficient social support to the development and maintenance of depressive symptoms 17. Two other known psychological interventions for depression, problem-solving therapy (PST) and psychodynamic therapy (PDT) were not included in the model because no trials could be found that exclusively focus on the prevention of relapse/recurrence in the continuation or maintenance phase.
A new (hypothetical) supported self-help intervention
Since existing therapist-led preventive psychological interventions might add too much pressure on already tight budgets, there is a demand for effective interventions that can be offered at low costs. Therefore we also evaluated the cost-effectiveness of a less costly type of CT, which is a supported self-help intervention with minimal guidance (henceforth: ‘supported self-help’). This supported self-help was recently developed \(^{18}\), but has not yet been evaluated in a cost-effectiveness trial. Since the effects of this supported self-help are not yet known, we simulated the minimum effectiveness needed for the self-help intervention to be able to successfully compete with the best alternative (i.e. the CT, MCT or ITP intervention).

Clinical evidence
We used clinical effectiveness data from the review by Biesheuvel-Leliefeld et al \(^{12}\) (Table 1). The outcome of interest was the relative risk (RR) with lower RR indicating a greater risk reduction for a depressive relapse.

### Table 1. Risk ratio and risk difference of psychological interventions versus treatment-as-usual (TAU)\(^{a}\) according to the random-effects model (DerSimonian and Laird)\(^{b}\)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>K</th>
<th>RR (95%CI)</th>
<th>Test</th>
<th>RD (95%CI)</th>
<th>NNT</th>
<th>I(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>9</td>
<td>0.68 (0.54;0.87)</td>
<td>(z=-3.12)</td>
<td>-0.196 (-0.28; -0.11)</td>
<td>5</td>
<td>52%</td>
</tr>
<tr>
<td>MCT</td>
<td>5</td>
<td>0.66 (0.53;0.82)</td>
<td>(z=-3.81)</td>
<td>-0.205 (-0.32; -0.09)</td>
<td>4</td>
<td>0%</td>
</tr>
<tr>
<td>IPT</td>
<td>3</td>
<td>0.41 (0.27;0.63)</td>
<td>(z=-4.10)</td>
<td>-0.160 (-0.37; -0.04)</td>
<td>6</td>
<td>0%</td>
</tr>
</tbody>
</table>

\(^a\) TAU in the meta-analysis is defined ‘routine clinical management, assessments only, no treatment and waiting-list control with unrestricted access to TAU.’

\(^b\) Abbreviations: CT, Cognitive (Behaviour) Therapy; CI, confidence interval; I\(^2\), heterogeneity; IPT, Interpersonal Therapy; K, number of studies; MCT, Mindfulness-based Cognitive Therapy; NNT, number-needed-to-treat; RD, risk difference; RR D-L, random-effects according to DerSimonian and Laird; TAU, treatment-as-usual

Costs
Costs were estimated by mapping the total time of one intervention (hours) multiplied by the appropriate full economic costs of the healthcare professional according to the Dutch guidelines for health economic evaluations \(^{19}\) (Table 2). Number of sessions and number of participants and time per session are based on commonly used formats. Costs of referral by a general practitioner were also included. Due to poor reporting, additional costs like costs of material, a possible orientation session or costs due to time spent by the patients at homework or travelling were not taken into account. Costs in euros (€) were converted to pounds sterling (£) using the purchasing power parities reported by the Organisation for
Economic Cooperation and Development, which convert currencies taking into account the differential buying power across countries. For the reference year 2013, €1 in The Netherlands was equal to a little over £0.84.

Table 2. Per patient costs of the interventions

<table>
<thead>
<tr>
<th></th>
<th>format</th>
<th>number of sessions</th>
<th>time per session (hours)</th>
<th>costs HCP per hour (€)</th>
<th>number of participants</th>
<th>referral costs GP (€)</th>
<th>total costs per patient (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>group</td>
<td>8</td>
<td>2</td>
<td>171</td>
<td>8</td>
<td>28</td>
<td>370</td>
</tr>
<tr>
<td>MCT</td>
<td>group</td>
<td>8</td>
<td>2</td>
<td>171</td>
<td>8</td>
<td>28</td>
<td>370</td>
</tr>
<tr>
<td>IPT</td>
<td>individual</td>
<td>12</td>
<td>1</td>
<td>171</td>
<td>1</td>
<td>28</td>
<td>2,080</td>
</tr>
<tr>
<td>self-help</td>
<td>individual</td>
<td>3</td>
<td>1</td>
<td>50</td>
<td>1</td>
<td>28</td>
<td>178</td>
</tr>
</tbody>
</table>

Abbreviations: CT, Cognitive (Behaviour) Therapy; HCP, healthcare professional; IPT, Interpersonal Therapy; MCT, Mindfulness-based Cognitive Therapy

Purchasing Power Parities (PPP) over 2013 were used for conversion from euro (€) to UK pound (£), found at the Organisation for Economic Cooperation and Development (OECD). http://stats.oecd.org/Index.aspx?DataSetCode=PPPGDP

Health economic evaluation using DepMod

DepMod is a health economic (Markov) model. It is developed and described in detail by Lokkerbol et al (2014). DepMod calculates the total healthcare costs and health gains by comparing a base-case scenario (enhanced TAU) with an alternative scenario (TAU plus an intervention). For the current study the alternative scenarios were defined as enhanced TAU plus CT, MCT, IPT or supported self-help.

DepMod assumes a population of 10 million people, aged 18-65 years. This population has an incidence of 158,000 new MDD cases per year with an episode duration of 6 months on average, and a prevalence of 588,600 acute cases annually. In this population, a rather conservative value of 45% of the currently depressed people have a history of previous episodes and are therefore seen as cases of recurrent depression. It should be noted that these epidemiological parameters are obtained from The Netherlands Mental Health Survey and Incidence Study 1 and 2 (NEMESIS 1 and 2), a population-based psychiatric epidemiologic cohort study. In this study, the time horizon is five years, standardised effect sizes are normally distributed, costs are gamma distributed and include only direct medical costs.

To allow for parameter uncertainty in costs and effects, the model randomly draws a value from the distributions assigned to the parameters and computes the outcome for that configuration of parameter values. This procedure is repeated 1,000 times over all parameters simultaneously. In each run, the outcomes (costs and health gains for each scenarios) are computed and stored in DepMod’s memory. Then, following the methods
of Briggs et al (2006) all 1,000 simulated outcomes are evaluated simultaneously, thus explicitly accounting for uncertainty in the input parameters. For more details on DepMod’s assumptions and their justifications we refer to Lokkerbol et al (2014).

**Sensitivity analysis**

One of the parameters in our health economic model is the coverage rate (%) of the interventions. In DepMod coverage rates can be used to conduct “what-if” analyses to evaluate the impact of adding or removing an intervention.

Empirical estimates of treatment coverage show much variation due to the availability of mental health services, cultural barriers that limit mental health service use etc. In the ESEMeD study 24, about one in three (36.5%) individuals with a 12-month prevalence of any mood disorder reported using health services. Andrews et al. (2004) found a coverage rate for depression of 31.7%. However, Chisholm et al. (2004) employed a coverage rate of 50% in his modelling study and in the Netherlands 58.5% of the people (aged 18-64 years) diagnosed with MDD, received some kind of treatment in the last year 27.

Given the modest levels of care-seeking and poor recognition rates of symptoms that precursor relapse, coverage rates of interventions aimed at the prevention of relapse or recurrence of depression, are assumed lower than those for acute depression. For example, coverage of e-health interventions for prevention of relapse and recurrence is set at 10% 13. In our study, the basic coverage rate is arbitrarily and conservatively set at 20% of the patients with a history of depression. In order to test the robustness of these results, the analysis will be repeated with a coverage rate of 40%. The results, based on this rather high coverage rate, will help us to better gauge the impacts of the new preventive interventions.

**RESULTS**

**Enhanced TAU**

When valuing each DALY averted at a WtP of €20,000 (£16,859), the healthcare system for the enhanced TAU scenario generates a value of €0.96 billion (£0.81 billion) (±50,000 DALY averted * €20,000) (95%CI: €0.91 – 1.01 billion) at an overall cost of €750 (£632) million. This results in a ROI of €1.30 (95%CI: €1.18-1.44) (£1.10, 95%CI: £0.99-1.21) (Table 3). While a ROI larger than 1 implies that enhanced TAU is cost-effective, it is important to realize that this value is used as a benchmark for the ROI of other scenarios with the new interventions included.
The following scenarios show the ROI of the added psychological interventions. As said before, in all scenarios the psychological intervention is offered to 20% of the patients with a history of depression and impacts are evaluated over a 5 year period.

**Scenario A: Preventive cognitive therapy**

The per-patient costs of CT of €370 (£312) do not put a lot of pressure on overall budget. When offering CT health care total expenditure increases with only 3.2%. With an average RR of 0.68 (95%CI:0.54-0.87), CT reduces the disease burden of major depression and leads to an increase in health effects of 13.8%. Since health effects increase more than costs, the ROI for adding CT increases from €1.30 to €1.43 (95%CI: €1.30-€1.58) (from £1.10 to £1.21, 95%CI: £1.10-£1.33).

**Scenario B: Interpersonal therapy**

IPT, being a labour-intensive intervention, has a per-patient cost of approximately €2,080 (£1,753) and places substantial pressure on budget. When offering IPT, spending increases with 23.3%. With an average RR of 0.41 (95%CI:0.27-0.63), IPT is effective in increasing health gains with 24.9%. Since costs and health effects increase by roughly the same amount, the ROI for adding IPT is more or less unaltered (€1.31; 95%CI: €1.20-1.45; £1.10, 95%CI: £1.01-1.22).

**Scenario C: Mindfulness-based cognitive therapy**

MCT, always offered in a group format, has a per-patient cost of approximately €370 (£312). When offering MCT health care expenditure increases with only 2.6%. With an average RR of 0.66 (95%CI:0.53-0.82), MCT is effective in reducing the disease burden and thus increases health gains with 14.5%. Since health effects increase more than costs, the ROI for adding MCT increases from €1.30 to €1.45 (95%CI: €1.31-1.60) (from £1.10 to £1.22, 95%CI: £1.10-1.35).

**Scenario D: supported self-help PCT**

Supported self-help, being an intervention that does not rely much on therapist’s time, has a per-patient cost of only €178 (£150). Our simulations indicate that the supported self-help intervention only needs to be moderately effective, with an RR of 0.71, to become as cost-effective as MCT, which showed the best ROI (€1.45; £1.22). This scenarios differs qualitatively from the previous scenarios in the sense that the effectiveness of this intervention is not yet known and we just determined the effectiveness threshold for supported self-help to become the most cost-effective approach.
Sensitivity analysis

In order to test the robustness of our results the coverage rate of 20% was increased to 40% as the highest attainable coverage. In this scenario, the ROI for IPT stays more or less the same (€1.33; 95%CI: €1.20-1.47; £1.12; 95%CI: £1.01-1.24). However, at a coverage rate of 40% the ROI of CT and MCT increases to €1.55 (95%CI: €1.41-1.71; £1.31; 95%CI: £1.19-1.44) and €1.58 (95%CI: €1.44-1.75; £1.33; 95%CI: £1.21-1.48) respectively. The minimum RR of the supported self-help, needed to compete with the highest ROI is a moderate 0.71.

Table 3. Overview of effects, costs and ROIs per intervention at different coverage rates

<table>
<thead>
<tr>
<th>Intervention</th>
<th>RR 95% CI</th>
<th>Costs per patient</th>
<th>ROI (€) 95% CI</th>
<th>ROI (£*) 95% CI</th>
<th>ROI (€) 95% CI</th>
<th>ROI (£*) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>20% coverage rate</td>
<td>40% coverage rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>enhanced TAU</td>
<td>n/a</td>
<td>n/a</td>
<td>1.30</td>
<td>1.10</td>
<td>1.30</td>
<td>1.10</td>
</tr>
<tr>
<td>CT</td>
<td>0.68</td>
<td>370</td>
<td>1.43</td>
<td>1.21</td>
<td>1.55</td>
<td>1.31</td>
</tr>
<tr>
<td></td>
<td>0.54-0.87</td>
<td></td>
<td>1.30-1.58</td>
<td>1.10-1.33</td>
<td>1.41-1.71</td>
<td>1.19-1.44</td>
</tr>
<tr>
<td>IPT</td>
<td>0.41</td>
<td>2.080</td>
<td>1.31</td>
<td>1.10</td>
<td>1.33</td>
<td>1.12</td>
</tr>
<tr>
<td></td>
<td>0.27-0.63</td>
<td></td>
<td>1.20-1.45</td>
<td>1.00-1.22</td>
<td>1.20-1.47</td>
<td>1.01-1.24</td>
</tr>
<tr>
<td>MCT</td>
<td>0.66</td>
<td>370</td>
<td>1.45</td>
<td>1.22</td>
<td>1.58</td>
<td>1.33</td>
</tr>
<tr>
<td></td>
<td>0.53-0.82</td>
<td></td>
<td>1.31-1.60</td>
<td>1.10-1.35</td>
<td>1.44-1.75</td>
<td>1.21-1.48</td>
</tr>
<tr>
<td>supported self-help</td>
<td>0.71**</td>
<td>178</td>
<td>1.45</td>
<td>1.22</td>
<td>1.44-1.75</td>
<td>1.21-1.48</td>
</tr>
</tbody>
</table>

*Purchasing Power Parities (PPP) over 2013 were used for conversion from euro (€) to UK pound (£), found at the Organisation for Economic Cooperation and Development (OECD). http://stats.oecd.org/Index.aspx?DataSetCode=PPPGDP

**Since the effects of this supported self-help are not yet known, we simulated the minimum effectiveness needed for the self-help intervention to be able to dominate the most cost-effective available intervention which is MCT with an ROI of €1.45 (20% coverage rate).

DISCUSSION

Main findings

This study aims to answer the following research questions:
1. Do preventive psychological interventions for recurrences in depressive disorder improve the cost-effectiveness over and above enhanced TAU?
2. What type of preventive psychological intervention makes the largest contribution in improving the health care system's cost-effectiveness?
3. At what effectiveness threshold becomes a hypothetical low-cost supported self-help intervention the preferred approach?
Chapter 4

The ROI of IPT (€1.31; 95%CI: €1.20-1.45; £1.10, 95%CI: £1.01-1.22) more or less equals the ROI of the base-case scenario of ‘enhanced TAU’ (€1.30; 95%CI: €1.18-1.44; £1.10, 95%CI: £0.99-1.21). However, CT and MCT are estimated to make the healthcare system more cost-effective with ROIs of €1.43 (95%CI: €1.30-1.58; £1.21, 95%CI: £1.10-1.33) and €1.45 (95%CI: €1.31-€1.60; £1.22, 95%CI: £1.10-1.35), respectively.

To produce a competitive ROI, the effectiveness of a hypothetical low-cost supported self-help intervention only needs to be successful in reducing the risk of a new depressive episode by a moderate RR of 0.71.

Adjusting the rather conservative coverage rate of 20% to a coverage rate of 40% does not impact the ROIs of IPT but makes CT and MCT even more attractive options for health care policy.

Strengths and limitations

In our study we used a Markov simulation model called DepMod. One of the benefits of a simulation model is that it makes it possible to conduct “if-then” analyses, allowing evaluation even of hypothetical interventions. This is helpful when exploring policy options by healthcare decision makers.

That said, our study has a number of limitations that need to be acknowledged.

First, in health economic modelling, much depends on the assumptions made in the model.

Assumptions in DepMod were as conservative as possible such that results are likely to portray not an overly optimistic outcome scenario. It should also be noted that the base-case scenario which forms the basis for the comparisons is an evidence-based healthcare system that is in full agreement with the Dutch clinical guidelines for the treatment of recurrent depression (enhanced TAU). This system is likely to be better than the current Dutch healthcare system. As a consequence, the ROI of the base-case scenario in this study (€1.30; £1.10) is likely to over-estimate the ROI of the present health care system for depressive disorders in the Netherlands.

Another limitation is that the current simulations are based on the Dutch population in the 18–65 year age bracket. Also the (enhanced) care scenario is modelled after the Dutch health care system for depressive disorders. Therefore, some caution should be applied when transferring our results to other countries.

Third, data on effectiveness of psychological interventions are drawn from a meta-analysis by Biesheuvel et al (2014). In this meta-analysis, preventive psychological interventions for recurrent depression are compared to TAU. The definition of TAU in this meta-analysis differs from the definition of ‘enhanced TAU’ in DepMod. The clinical data on effectiveness of the preventive psychological interventions that are used in the model are therefore probably too optimistic.
Fourth, in our study we did not include the implementation costs of changing from the current health care system to an alternative scenario. Instead, we looked at “steady state” scenarios, after implementation and asked ourselves what scenario would then be most appealing from a cost-effectiveness point of view.

Finally, owing to poor reporting, some aspects of the new interventions like costs of materials (e.g. therapy books) or costs due to time spent by the patients at e.g. homework or travelling, were not taken into account. As a consequence, the ROI of all scenarios is overestimated.

**Implications for practice**

Only few studies on cost-effectiveness of psychological interventions for the prevention of depression have been published 28–33. From a health care perspective, all these economic evaluations show that preventive psychological interventions may represent good value for money versus TAU and/or ADM. Our study adds to this by showing that CT and MCT have the potential to improve the cost-effectiveness of the healthcare system. Due to the current economic down-turn, the squeeze on government budgets, and an expenditure for mental health care that is unlikely to be sustainable 34, governments are forced to allocate resources to these interventions that are seen to maximise cost-effectiveness.

Besides cost-effectiveness, patients' preferences also play an important role in choosing one intervention over another. Currently, maintenance antidepressants are the mainstay approach for the prevention of relapse or recurrence. However, many patients express a preference for psychosocial interventions that provide long-term protection against relapse or recurrence.

Based on both cost-effectiveness and preference, a widespread introduction of MCT and CT may thus be preferred but poses a great challenge; currently, most depression is treated in primary care where there is a lack of cognitive therapists. Therefore, access to these therapies could only improve if primary care health nurses are trained to support the self-help interventions in primary care. Studies already showed that mental health nurses provide high quality psychological interventions in primary care if they are closely supervised by experienced therapists in a collaborative care model 35–37. As a positive side-effect, costs would even decrease and thus improve ROI.

Finally, this study showed that the hypothetical low-cost supported self-help may be a potentially attractive alternative. However, the exact role of the nurse, duration of treatment and follow-up and type of contact (telephone/internet/face-to-face) all require empirical support. More research should demonstrate the actual value of this intervention.
REFERENCES


