CHAPTER FIVE

Cost–effectiveness of the Intervention

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Cost–effectiveness of an Internet–based pre–treatment for phobic outpatients: multi-
centre randomised controlled trial.
ABSTRACT

BACKGROUND — Phobias are among the most common anxiety disorders encountered in outpatient mental health clinics. Although Internet-based treatments have been investigated in primary care and the general population and are increasingly used in clinical practice, little is known about the cost-effectiveness of Internet-based guided self-help as a precursor to face-to-face psychotherapy as compared to usual care.

METHODS — Eight Dutch outpatient clinics participated in a randomised controlled multi-centre trial. We included adult patients from outpatient clinics’ waiting lists with social anxiety, agoraphobia and/or specific phobias. Those suffering from psychotic disorders or at risk of suicide were excluded. Randomisation was performed by an external researcher, stratified by clinic, in blocks of eight. Patients and clinicians were not blind to patient allocation, and assessments were performed through the Internet. Patients were allocated to either a five-week Internet-based guided self-help programme followed by face-to-face psychotherapy or remained on the clinic waiting list and received face-to-face psychotherapy at the end of the waiting list period. The primary clinical outcome measure was the Fear Questionnaire at 12-month follow-up. Costs were measured from a societal perspective using the iMTA Questionnaire on Costs Associated with Psychiatric Illness. Primary analyses were performed on an intention-to-treat basis.

FINDINGS — Between August 2010 and October 2013, we screened 481 patients for eligibility, of whom 212 patients were randomly assigned to either the Intervention (105) or control group (107). At 1-year follow-up, no significant differences in the primary outcome (mean difference FQ –3.51, p = .383; d=–0.15; 95% CI –11.51 to 4.46) or total costs from a societal perspective (mean difference = –€481, 95% CI €–1343 – €4401) were found. Although on average patients in the intervention group used fewer face-to-face psychotherapy sessions, this difference was not statistically significant (mean difference = –4.81 sessions, 95% CI –2.22–11.83, p=.180). The adherence to the intervention was low, with only 13.3% of 105 patients completing all five weeks of the intervention. No adverse events were reported.
INTERPRETATION — Using Internet–based guided self–help as a precursor to face–to–face psychotherapy was not cost–effective from a societal perspective. Although intervention participants appeared to use fewer face–to–face psychotherapy sessions, this result was not statistically significant. Differences in costs and effects between the intervention group and care as usual were minimal. Implementation of this intervention may be beneficial to patients, but not cost–effective in its current iteration.
INTRODUCTION

Phobias are highly prevalent. The prevalence rate for social phobia, agoraphobia and specific phobias together is estimated to be around 18 (De Graaf, Ten Have, Van Gool, & Van Dorsselaer, 2012), and all have a considerable impact on the daily life of patients (Depla, ten Have, van Balkom, & de Graaf, 2008; Mendlowicz & Stein, 2000). The prevalence and the impact of phobias are often underestimated (Weiller, Bisserbe, Boyer, Lepine, & Lecrubier, 1996). For example, research shows that the burden of agoraphobia is higher even than that of major depression (Smit et al., 2006). The per capita costs for phobia are relatively low, but because of the high prevalence and reduced quality of life, the overall public health burden and societal costs are high (Konnopka, Leichsenring, Leibing, & König, 2009; Smit et al., 2006). Psychotherapy, using the principles of cognitive behavioural therapy and exposure therapy, is generally accepted as the preferred treatment for all types of phobias (Acarturk, Cuijpers, van Straten, & de Graaf, 2009; Kok et al., 2017; Sánchez–Meca, Rosa–Alcázar, Marín–Martínez, & Gómez–Conesa, 2010).

A new modality which is currently gaining acceptance is web–based guided self–help, in which a patient individually works through a treatment with support from a therapist. In this treatment, psychotherapeutic principles are explained to the patient in a number of lessons and every lesson ends with some form of homework assignments. In these interventions, homework assignments appear to be effective components (Kazantzis, Deane, & Ronan, 2000), and especially exposure homework exercises were found to be a good predictor of favourable treatment outcome (Al–Kubaisy et al., 1992; Cammin–Nowak et al., 2013; Edelman & Chambless, 1993). To assist the patient in completing the web–based therapy, therapist guidance is provided over the Internet. This guidance is aimed at motivating patients to proceed and explaining therapeutic principles or assignments in detail if needed.

To date, non–web–based guided self–help based on the principles of exposure has been found to be effective for social phobia, agoraphobia and specific phobias (Cuijpers, Donker, van Straten, Li, & Andersson, 2010; Hirai & Clum, 2006). In community samples, it was found to be as effective.
as face-to-face (FtF) psychotherapy (Cuijpers et al., 2010). Non-web-based
guided self-help has usually been offered through a book (bibliotherapy),
but in the past decade online treatment has been increasingly replacing
classic bibliotherapy, and some evidence exists that internet-based guided
self-help treatments are cost-effective when compared to control treat-
ments (Donker et al., 2015).

In the Netherlands, patients with a severe phobia are generally referred
to an outpatient mental health clinic by their GPs for face-to-face (FtF)
psychotherapy. At these outpatient clinics, patients are placed on a waiting
list, the length of which varies depending on therapist load availability, but
is usually at least six weeks. In theory, patients could make effective use of
this time spent waiting for FtF psychotherapy by completing homework
exercises.

As Internet-based guided self-help interventions have generally been
shown to be effective (Andersson, Cuijpers, Carlbring, Riper, & Hedman,
2014; Cuijpers et al., 2009), we hypothesized that offering a guided Internet-
based intervention to outpatients prior to regular FtF therapy would lead
to lower treatment costs by way of fewer FtF sessions, and a faster recovery.

During the Internet-based intervention, patients gain knowledge about
their disorder and exposure therapy, and acquire skills that are normally
taught during the first sessions of FtF psychotherapy.

We undertook a trial to assess whether offering web-based guided self-
help during the waiting list period could be (cost)effective in comparison to
care as usual. Previously, short-term clinical results (5 weeks) showed
that this Internet intervention had modest effects on phobia symptoms
with a Cohen’s d of 0.3 (Kok, van Straten, Beekman, & Cuijpers, 2014) in
comparison to patients who received no specific intervention while on the
waiting list.

The current paper describes the 12-month effectiveness and cost-effec-
tiveness of the guided Internet intervention preceding FtF psychotherapy
versus waiting list preceding FtF psychotherapy from a societal perspective.
METHODS

PATIENT SELECTION AND INCLUSION

Eight outpatient clinics in large cities in the west of the Netherlands participated. We recruited outpatients from clinic waiting lists and conducted an economic evaluation from a societal perspective alongside a randomised controlled trial (Kok et al., 2012, 2014) with a 12-month follow-up period. A detailed description of the design has been published elsewhere (Kok et al., 2012). The study protocol has been approved by the Medical Ethical Committee of the VU University Medical Centre. Patients were referred to the research team by the outpatient clinic staff after an initial telephone contact with the patient. During this telephone call, outpatient staff screened whether phobic complaints were the main reason for seeking help and asked patients for consent to be contacted by the research team. If the patient consented, the research team contacted the patient for a structured clinical diagnostic interview (CIDI; World Health Organization, 1990) by telephone to determine eligibility, after which formal written informed consent was obtained and baseline measures were administered. Computer-literate, Dutch-speaking patients, 18 years or older, with a DSM–IV–TR or ICD–10 diagnosis of a phobia (social phobia, agoraphobia or any type of specific phobia) were eligible for inclusion. Stable psychotropic medication use was allowed. Patients with psychotic disorders or an elevated risk for suicide were excluded and remained on the waiting list for treatment.

RANDOMISATION

Patients were randomised by a researcher not involved in the project, using a computer-generated randomisation list stratified by outpatient clinic, with blocks of 8 patients. After baseline measurements, included patients were randomised to either a) receive immediate access to a 5-week guided Internet-based self-help programme followed by FtF treatment (intervention), or b) remain on the outpatient clinic waiting list followed by FtF treatment (control).
INTERVENTION

The five-week Internet-based intervention was based on a self-help book based on exposure therapy for phobic patients (de Neef & Cuijpers, 2007), written by an experienced cognitive-behavioural therapist. This program was adapted by the researchers for the Internet, resulting in an intervention consisting of 5 lessons.

In the first lesson, patients read psycho-educational material. During week 2, patients identify key fears, establish a fear hierarchy and build an exposure exercise planning. In weeks 3 and 4, patients exercise self-exposure according to their fear hierarchies. In week 5, patients learn strategies to prevent relapse, continue to plan for self-exposure and anticipate FtF psychotherapy. Each week, the patient reported back to the coach with achievements, questions or for general support.

Master’s level clinical psychology students were trained to deliver guidance during the intervention. The coaches monitored the patient’s progress through the intervention, encouraged the patient to persist through the intervention, and provided feedback on the homework assignments. Coaches spent approximately 15 minutes per week per patient and were supervised by the first author (RK) as well as the first author of the self-help book.

Throughout the intervention period, patients remained on the waiting list for FtF psychotherapy to ensure that they did not experience any delay in receiving scheduled FtF psychotherapy.

After patients finished the Internet treatment or 6 weeks after randomisation (whichever occurred first), the researchers inserted a short, written report into the patient’s electronic health record (EHR) to inform therapists about the progress the patient had made during the Internet treatment.

Therapists were encouraged to tailor FtF treatment to the progress the patient had made during the Internet intervention. As a consequence, FtF therapists were not blinded to treatment status. Therapists and coaches were not involved in outcome assessments.
CONTROL GROUP

Patients in the waiting list control group remained on the waiting list for FtF psychotherapy and received FtF psychotherapy as scheduled. Additionally, the control group received the self-help book on which the Internet intervention was based. This book was sent to the control group patients free of charge, with no instructions or support. Therapists who delivered subsequent FtF therapy were aware that the patient was a control patient in the trial.

SUBSEQUENT FTF PSYCHOTHERAPY

Every patient received psychotherapy as usual after the waiting list period or receiving the Internet intervention, unless the patient explicitly opted out of treatment. As in routine clinical practice, treatment type (i.e., individual FtF therapy or group therapy with or without pharmacotherapy) for each patient was a joint decision between the patient and the therapist, depending on symptom severity, type of phobia and patient preference.

Cost outcome measures Costs were assessed from a societal perspective using an adapted version of the iMTA Questionnaire on Costs Associated with Psychiatric Illness (TiC–P; Hakkaart-van Roijen, 2002) with a recall period of 3 months, over a total period of 12 months. Cost categories included direct medical costs (use of health services and medication), direct non-medical costs (informal care) and indirect non-medical costs (absenteeism and presenteeism).

Dutch standard costs were used to value health utilization, informal care and lost work productivity. The friction cost method was used to estimate work absenteeism costs based on Dutch age and sex specific productivity costs. A friction period of 23 weeks was use (Hakkaart-van Roijen, Tan, & Bouwmans, 2011). All costs were corrected to 2012 levels consumer price indices (Statistics Netherlands, 2012). The number of visits to the outpatient clinics was obtained from the institutions’ electronic health records (EHRs). Patient-level data retrieved from the EHRs included number of sessions of psychotherapy; type of psychotherapy; modality (group or individual), and number of health providers (therapists, assistants, etc.)
and patients involved. Costs for a session of group therapy was also based on Dutch standard costs (Hakkaart–van Roijen et al., 2011) but adjusted pragmatically for number of attending therapists and patients per session.

**CLINICAL OUTCOME MEASURES**

Outcomes were assessed through online questionnaires. In case of non–response, the research team sent reminder e–mails followed by reminder telephone calls. Outcome measures were recorded at baseline, at 5 weeks and 3, 6, 9 and 12 months after randomisation.

The primary outcome measure was the Fear Questionnaire (FQ; Marks & Mathews, 1979), which measures phobic fear and avoidance on a 15–120 scale, where higher scores indicate more severe phobic symptoms. Secondary outcome measures included symptoms of anxiety and depression, quality of life and the number of FtF therapy sessions. Anxiety symptoms were measured by the Beck Anxiety Inventory (BAI; Beck & Steer, 1993), score range 0 — 63, where higher scores indicate more anxiety.

Depressive symptoms were measured by the CES–D (Radloff, 1977; score range, (0 – 60), where higher scores correspond to more depressive symptoms. Quality of life was measured using the Euroqol (EuroQol Group, 1990; EQ–5D). EQ–5D health states were converted to utilities using the Dutch tariff (Lamers, Stalmeier, McDonnell, Krabbe, & van Busschbach, 2005). Quality–adjusted life years (QALYs) were calculated by multiplying the EQ–5D utilities by the time spent in that particular health state and interpolating linearly between follow–up measurements.

**ANALYSES**

Based on large effect sizes found in the general population (Cuijpers et al., 2009), we assumed a conservative mean standardised effect size (Cohen’s d) of 0.7 in the intervention group in clinical practice. As such, 170 patients were needed to obtain 90% statistical power with a 2–sided alpha = .05. Anticipating 30% drop–out over 12 months, we aimed to include 244 patients. Nationwide changes to the insurance system caused enrolment in all outpatient clinics to decline during patient accrual. Thus, we included 212 patients between
July 2010 and December 2013. All statistical analyses were performed on an intention-to-treat (ITT) basis. Missing data were imputed using multiple imputation (MI) with fully conditional specification and predictive mean matching as implemented in SPSS version 21. Predictor variables related to missingness were included in the imputation model. Fifty imputed datasets were needed to reach a loss of efficiency smaller than 5%. For the cost-effectiveness analyses, 50 separate data sets were created and analysed using STATA 13.0 (Statacorp LP, 2013), and the results were pooled using Rubin’s rules (Wiley & Rubin, 1987). Bivariate regression models were used to evaluate the differences in costs and effects between the intervention groups, while maintaining the correlation between costs and effects. Effect differences were adjusted for baseline values. We calculated incremental cost-effectiveness ratios (ICERs) by dividing the difference in clinical effectiveness between intervention and waiting list control groups by the difference in costs between these two groups (\[\text{ICER} = \frac{\Delta E}{\Delta C}\]).

Bias-corrected accelerated bootstrapping (5000 replications) was used to estimate uncertainty surrounding the cost differences and the ICERS. Outliers in cost data were identified by calculating the Mahalanobis distances total costs as predictors as implemented in SPSS 21. Cases thus identified as being significant positive outliers (N=3; two intervention patients and one control group patient) were removed. No negative outliers were observed.

Bootstrapped cost-effect pairs are presented graphically on a cost-effectiveness (CE) plan (Black, 1990). On a CE-plane, uncertainty around incremental costs (y-axis) and incremental effects (x-axis) is summarised graphically. Each bootstrapped estimate is placed along four separate quadrants; more expensive and more effective (NE quadrant), less expensive and more effective (SE), less effective and less expensive (SW), and more expensive and less effective (NW). The SE quadrant is most desirable, as the new intervention dominates the control condition by being more effective and less expensive. Conversely, the NW quadrant is least desirable as the new intervention is dominated by the control condition by being less effective and more expensive. In the two remaining quadrants, decision makers need to justify either a less expensive but less effective intervention (SW quadrant)
or a more effective but more expensive intervention (NE quadrant). In the latter scenario, a decision has to be made whether the higher costs weigh up against the additional benefits. This decision depends on the societal willingness to pay (WTP), i.e. how much money society is willing to pay for one additional unit of effect. Since it is generally unknown how much society is willing to pay, different WTP–scenarios are plotted on a cost–effectiveness acceptability (CeA) curve, which graphically represents the probability that the intervention is cost–effective in comparison with control (Y–axis) for a range of hypothetical societal WTP values (X–axis).

Per–protocol analyses

For the per–protocol analyses, patients who had not started the web–based intervention or had not completed the first week (N = 23) were omitted from the analyses.

RESULTS

DESCRIPTION OF THE SAMPLE & DROP–OUT

Between August 26th 2010 and October 17th 2013, we assessed 481 outpatients for eligibility, of whom 153 (31.8%) declined to participate, 111 (23.0%) did not meet inclusion criteria, and 5 (1.0%) could not be contacted after initial screening. The remaining 212 patients were randomised to either the Internet treatment during the waiting list period (N=105) or control (waiting list alone; N=107, see Figure 5.1). The sample was slightly skewed toward the female gender (61.0%) and those with higher education (57.1%). Patients were recruited at outpatient clinics of PSYQ, GGZ ingeest, Prezens, GGZ Noord–Holland–Noord and Altrecht. Most patients (78%) were recruited at the PSYQ outpatient clinics. Due to database issues, baseline measurements were unavailable for 2 out of 212 patients.

Furthermore, details on FtF–therapy attendance could not be retrieved for 8 intervention patients and 6 control group patients. Clinical data on 210
patients was used for the intention–to–treat analyses. Of the intervention group, 56 patients completed the 5–week post–test assessment (53.3%) and of the control group, 72 completed the post–test assessment (67.3%).

FIGURE 5.1 — Participant flowchart
At the one-year follow-up mark, 42 intervention patients (40.0%) and 52 control group patients (48.6%) completed the follow-up measures (i.e., were completers). As described in detail elsewhere (Kok et al., 2014), non-completers differed significantly from responders and had higher baseline depression and anxiety scores, were younger, had lower education and were on psychotropic medication more often.

### TABLE 5.1 — Baseline characteristics.

<table>
<thead>
<tr>
<th></th>
<th>TOTAL SAMPLE (N=212)</th>
<th>INTERVENTION + PSYCHOTHERAPY (N=105)</th>
<th>CONTROL + PSYCHOTHERAPY (N=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEMOGRAPHICS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>34.6 (11.7)</td>
<td>35.7 (11.7)</td>
<td>33.4 (11.6)</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>130 (61%)</td>
<td>58 (55%)</td>
<td>72 (67%)</td>
</tr>
<tr>
<td>Higher Education¹, N (%)</td>
<td>120 (57%)</td>
<td>58 (56%)</td>
<td>62 (58%)</td>
</tr>
<tr>
<td>Single, N (%)</td>
<td>112 (53%)</td>
<td>55 (53%)</td>
<td>57 (53%)</td>
</tr>
<tr>
<td>Income², mean (SD)</td>
<td>€1524 (€761)</td>
<td>€1545 (€727)</td>
<td>€1503 (€796)</td>
</tr>
<tr>
<td><strong>BASELINE SCORES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FQ (mean, SD)</td>
<td>40.28 (22.71)</td>
<td>42.43 (23.41)</td>
<td>38.19 (21.93)</td>
</tr>
<tr>
<td>BAI (mean, SD)</td>
<td>44.81 (13.41)</td>
<td>45.15 (13.76)</td>
<td>44.48 (13.13)</td>
</tr>
<tr>
<td>CES-D (mean, SD)</td>
<td>24.82 (8.47)</td>
<td>24.96 (8.61)</td>
<td>24.69 (8.37)</td>
</tr>
<tr>
<td>EQ-5D (mean, SD)</td>
<td>0.57 (0.27)</td>
<td>0.60 (0.28)</td>
<td>0.55 (0.27)</td>
</tr>
<tr>
<td>Currently using psychotropic medication, N (%)</td>
<td>43 (20%)</td>
<td>14 (13%)</td>
<td>29 (27%)</td>
</tr>
</tbody>
</table>

¹ Equivalent to a bachelor’s degree or higher
² N = 180; monthly disposable income; 2012 €

### UPTAKE OF THE INTERNET & FTF INTERVENTIONS

Of the 105 patients allocated to the intervention, 86 (78.1%) started and 14 (13.3%) completed all five weeks of the intervention. On average, patients completed 3.6 out of 8 exercises (SD 2.6, median number of completed exercises 3; range 0–8). All but 4 patients received the scheduled FtF psychotherapy after waiting list (n=2) or intervention (n=2). At 12-month follow-up,
patients had received an average of 25.8 sessions of FtF psychotherapy (group sessions and individual sessions combined). Intervention patients used on average 23.3 sessions of FtF psychotherapy and control patients used 25.8 sessions of FtF psychotherapy. This difference was not statistically significant (95% CI of difference, –2.22;11.83).

Of all patients for whom FtF data were available (N=196); 26.0% received fewer than 10 sessions, 24.0% received 10–19 sessions, 16.3% received 20–29 sessions, 12.2% received 30–39 sessions and 21.5% received more than 40 sessions of FtF psychotherapy. Combined individual and group treatment was received by 110 (56.1%) of patients, whereas 63 (32.1%) patients received only individual treatment and 10 (5.1%) patients received only group therapy. On average, patients received 13.3 individual sessions and 12.5 group sessions. No significant differences were observed in modality of therapy (individual vs. group therapy) received by the intervention and control group patients (table 5.2). Additionally, there was no significant difference in number of FtF therapy sessions received by patients that did not start the intervention at all when compared to patients that did start the intervention (p = .093), but patients that never started using the intervention had significantly higher baseline anxiety levels than patients that did start using the intervention (mean difference 7.1 points on the BAI, p = .029).

CLINICAL OUTCOMES AT FOLLOW–UP

The imputed outcomes at 1–year follow–up are presented in table 5.2. At 1–year follow–up, there were no statistically significant differences in clinical outcomes between the intervention and control groups (mean difference FQ –3.51, p = .383; d=–0.15; 95% CI –11.51 to 4.46).

As shown in figure 5.2, both the intervention and control groups appear to follow the same general pattern of improvement over time when compared to baseline scores. The intervention group improved more than the control group during the intervention period (between baseline and 5 weeks of follow–up). However, this difference disappeared as time progressed. Additionally, there were no statistically significant differences in secondary outcomes between the intervention and control groups (table 5.2).
TABLE 5.2 — Clinical outcomes at 1-year follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Intervention &amp; psychotherapy (N=104)</th>
<th>Control &amp; psychotherapy (N=106)</th>
<th>Between groups difference</th>
<th>Effect size d (95% CI around d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FQ (M/SD)</td>
<td>31.53 (24.12)</td>
<td>28.02 (22.56)</td>
<td>-3.51</td>
<td>-0.15 (−11.51 to 4.46)</td>
</tr>
<tr>
<td>BAI (M/SD)</td>
<td>38.73 (13.42)</td>
<td>38.01 (13.71)</td>
<td>-0.72</td>
<td>-0.06 (−4.95 to 3.59)</td>
</tr>
<tr>
<td>CES-D (M/SD)</td>
<td>18.24 (15.24)</td>
<td>17.98 (14.80)</td>
<td>-0.26</td>
<td>-0.02 (−5.44 to 4.91)</td>
</tr>
<tr>
<td>QALY (M/SD)</td>
<td>0.57 (0.16)</td>
<td>0.57 (0.15)</td>
<td>0.02</td>
<td>-0.04 (−0.05 to 0.05)</td>
</tr>
</tbody>
</table>

Clinical scores at 1-year follow-up, imputed intention–to–treat sample

<table>
<thead>
<tr>
<th></th>
<th>Control + FtF</th>
<th>Intervention + FtF</th>
</tr>
</thead>
<tbody>
<tr>
<td>FQ (M/SD)</td>
<td>30.72 (23.33)</td>
<td>28.04 (22.66)</td>
</tr>
<tr>
<td>BAI (M/SD)</td>
<td>38.01 (12.60)</td>
<td>38.07 (13.70)</td>
</tr>
<tr>
<td>CES-D (M/SD)</td>
<td>17.17 (14.53)</td>
<td>17.98 (14.86)</td>
</tr>
<tr>
<td>QALY (M/SD)</td>
<td>0.62 (0.18)</td>
<td>0.64 (0.15)</td>
</tr>
</tbody>
</table>

Clinical scores at 1-year follow-up, imputed per protocol sample

FIGURE 5.2. Change in Fear Questionnaire scores between the intervention and control group over time.
## Table 5.3 — Psychotherapy use and costs at 1-year follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Unit Cost</th>
<th>Intervention Group</th>
<th>Control Group</th>
<th>Difference (95% CI of Difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of FtF sessions (M/SD)</td>
<td>—</td>
<td>23.34 (21.25)</td>
<td>28.15 (28.26)</td>
<td>−4.81 (−2.22 to 11.83)</td>
</tr>
<tr>
<td>——individual sessions (M/SD)</td>
<td>€181.50</td>
<td>12.22 (9.98)</td>
<td>14.34 (14.78)</td>
<td>−2.12 (−1.42 to 5.67)</td>
</tr>
<tr>
<td>——group sessions (M/SD)</td>
<td>€96.31b</td>
<td>11.13 (15.22)</td>
<td>13.81 (19.47)</td>
<td>−2.69 (−2.22 to 7.59)</td>
</tr>
<tr>
<td>FtF no shows (M/SD)</td>
<td>€181.50c</td>
<td>1.95 (3.39)</td>
<td>1.85 (2.87)</td>
<td>0.10 (−0.98 to 0.78)</td>
</tr>
<tr>
<td>Internet intervention costs</td>
<td>d</td>
<td>€252 (€9)</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Psychotherapy costs (M/SD)</td>
<td>—</td>
<td>€3732 (€3004)</td>
<td>€4163 (€4043)</td>
<td>€ −431 (€ −536 to €1398)</td>
</tr>
<tr>
<td>Other health costs (M/SD)</td>
<td>—</td>
<td>€8623 (€5294)</td>
<td>€8698 (€6121)</td>
<td>€ −75 (€ −1688 to €1838)</td>
</tr>
<tr>
<td>Sick leave (€) (M/SD)</td>
<td>—</td>
<td>€123 (€349)</td>
<td>€411 (€1294)</td>
<td>€ −289 (€ −33 to € −544)</td>
</tr>
<tr>
<td>Indirect costs (M/SD)</td>
<td>—</td>
<td>€1884 (€2178)</td>
<td>€1799 (€2310)</td>
<td>€ 85 (€ −1076 to €906)</td>
</tr>
<tr>
<td>Total societal costs (M/SD)</td>
<td>—</td>
<td>€12355 (€7653)</td>
<td>€12861 (€9576)</td>
<td>€ −505 (€ −1343 to €4401)</td>
</tr>
</tbody>
</table>

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*a Index year = 2012

*b Unit cost derived from an average in this data set. Due to varying numbers of patients and care givers per session, unit prices for group sessions will vary.

c A no-show, or an appointment missed without prior notification by the patient, was valued at one session of FtF psychotherapy due to lost productivity of the therapist.

d Costs may vary according to the time spent per client by the online therapist.
COSTS

Table 5.3 presents F2F psychotherapy use, societal and health costs of all patients. The mean intervention costs were €252 (SD €9) per intervention patient, based on actual costs of the intervention itself and average wages for master’s level student coaches.

About one-thirds of health costs was attributable to psychotherapy and two-thirds to use of other health services.

Lost productivity costs due to absenteeism and presenteeism were lower than total health care costs. On average, the intervention group was absenting on sick leave for 26.96 hours (SD 21.12 hours) as opposed to 30.75 hours (SD 45.92) in the control group (95% CI −0.79 to 9.56).

In the intention-to-treat analysis, the intervention resulted in a statistically non-significant average societal cost reduction of €481 as compared to control. In the per-protocol analysis, this reduction was €1525, but this was also not statistically significant.

COST-EFFECTIVENESS ANALYSES

Table 5.4 presents the results of the cost-effectiveness analyses for both the intention-to-treat and per-protocol analyses. For the FQ in the intention-to-treat analysis, the ICER was 166, which indicates that a deterioration of 1 point on the FQ was associated with €166 lower costs.

The majority of the bootstrapped cost-effect pairs were situated in the south-west quadrant of the cost-effectiveness plane; indicating lower costs and slightly smaller effects (Table 5.4 & Figure 5.3).

The cost-effectiveness acceptability curve for FQ shows that at a WTP of €0 per point improvement on the FQ, there is a 0.65 probability that the intervention is cost-effective in comparison with control.

The probability of cost-effectiveness decreases with increasing values for WTP, due to the total costs for the intervention group being lower than for the control group. Results for secondary outcome measures were similar.

In the per-protocol analysis, bootstrapped cost-effect pairs for the FQ were also mainly situated in the south-west quadrant (Table 5.4 & Figure
The CEA curves show that the probability of cost-effectiveness is 0.86 at a WTP of €0 per point improvement and decreases with increasing values for WTP (Figure 5.4). Similar results were found for the secondary outcome measures.

### Table 5.4 — Results of the cost-effectiveness analyses.

#### Intention to treat sample (N=210); outliers removed

<table>
<thead>
<tr>
<th></th>
<th>Δ Costs (95% CI, 2012 €)</th>
<th>Δ Effects (95% CI)</th>
<th>ICER</th>
<th>NE (%)</th>
<th>SE (%)</th>
<th>SW (%)</th>
<th>NW (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FQ</td>
<td>-€481 (-€3127 to €1923)</td>
<td>-3.52 (-10.6 to 4.8)</td>
<td>166</td>
<td>7</td>
<td>17</td>
<td>48</td>
<td>29</td>
</tr>
<tr>
<td>BAI</td>
<td>-€481 (-€3127 to €1923)</td>
<td>-0.72 (-4.9 to 3.4)</td>
<td>601</td>
<td>13</td>
<td>23</td>
<td>42</td>
<td>23</td>
</tr>
<tr>
<td>CES-D</td>
<td>-€481 (-€3127 to €1923)</td>
<td>-0.26 (-5.6 to 4.7)</td>
<td>1203</td>
<td>13</td>
<td>30</td>
<td>35</td>
<td>22</td>
</tr>
<tr>
<td>QALY</td>
<td>-€481 (-€3127 to €1923)</td>
<td>-0.02 (-0.04 to 0.05)</td>
<td>102975</td>
<td>22</td>
<td>37</td>
<td>29</td>
<td>13</td>
</tr>
</tbody>
</table>

#### Per protocol sample (N=171); outliers removed

<table>
<thead>
<tr>
<th></th>
<th>Δ Costs (95% CI, 2012 €)</th>
<th>Δ Effects (95% CI)</th>
<th>ICER</th>
<th>NE (%)</th>
<th>SE (%)</th>
<th>SW (%)</th>
<th>NW (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FQ</td>
<td>-€1525 (-€4301 to €1204)</td>
<td>-3.1 (-11.7 to 5.4)</td>
<td>491</td>
<td>2</td>
<td>21</td>
<td>65</td>
<td>11</td>
</tr>
<tr>
<td>BAI</td>
<td>-€1525 (-€4301 to €1204)</td>
<td>-0.8 (-5.4 to 3.8)</td>
<td>1906</td>
<td>5</td>
<td>31</td>
<td>55</td>
<td>9</td>
</tr>
<tr>
<td>CES-D</td>
<td>-€1525 (-€4301 to €1204)</td>
<td>0.3 (-5.1 to 5.8)</td>
<td>5083</td>
<td>6</td>
<td>48</td>
<td>38</td>
<td>7</td>
</tr>
<tr>
<td>QALY</td>
<td>-€1525 (-€4301 to €1204)</td>
<td>-0.01 (-0.06 to 0.05)</td>
<td>93762</td>
<td>7</td>
<td>36</td>
<td>51</td>
<td>8</td>
</tr>
</tbody>
</table>
FIGURE 5.3 — Intention-to-treat cost-effectiveness plane and corresponding cost-effectiveness acceptability curve for primary outcome measure Fear Questionnaire.
FIGURE 5.4. Per protocol cost–effectiveness plane and corresponding cost–effectiveness acceptability curve for primary outcome measure Fear Questionnaire.
DISCUSSION

The aim of this study was to assess the effectiveness and cost-effectiveness of offering web-based guided self-help to phobic outpatients during waiting list.

We hypothesized that implementing the Internet intervention during the waiting list period would result in similar or larger clinical effects while simultaneously reducing costs. In a previous paper, we demonstrated that the intervention was moderately effective after 5 weeks (Cohen’s $d = 0.35$) in comparison with a waiting list condition as a precursor to FtF treatment (Kok et al., 2014). However, this paper shows that there were no statistically significant differences in clinical outcomes between the intervention and control group at 12-month follow-up.

Patients in the intervention group used fewer sessions of FtF psychotherapy than the control group, although this difference was not statistically significant. Total societal costs were slightly and non-significantly lower in the intervention group than in the control group which was mainly due to the lower number of FtF psychotherapy sessions. There appeared to be an association between the uptake of the intervention and the number of FtF sessions used.

Based on the results of this study we conclude that the internet intervention is not cost-effective in comparison with control for patients with phobias on a waiting list for psychotherapy. Despite there being no statistically significant difference in clinical effects at 12-month follow-up, the intervention group used 4.8 FtF sessions fewer than the control group (23.4 in the intervention group vs 28.2 in the control group).

Taking into account the average of 2 hours’ coaching time to guide patients through the Internet intervention, the approximate total reduction in therapist time was 10%. Although this difference was not statistically significant, outpatient clinics consider this is a clinically relevant decrease in treatment time.

Improving adherence to the intervention may result in a larger reduction in therapist time.
A major limitation of this study is that the uptake of the Internet intervention was very low. This may be the result of a number of factors. Although we did not record reasons to discontinue the intervention, reasons for dropping out may be related to the content or design of the intervention (Kelders, Kok, Ossebaard, & Van Gemert-Pijnen, 2012), the design or implementation of the study itself or other nonspecific factors. It should be noted that patients in both conditions were referred to the outpatient clinics, expecting to receive FtF psychotherapy. This expectation may have caused patients to discontinue the Internet intervention prematurely, as patient expectation has been shown to influence adherence (Boettcher, Renneberg, & Berger, 2013) and patients were scheduled to receive psychotherapy regardless of whether they participated in the online intervention.

Secondly, patient recruitment was not fully embedded within outpatient clinics, as the trial was coordinated from an academic setting and not from the clinics. Embedding the intervention by collaborating more proactively with FtF therapists may improve intervention adherence and consequently, clinical outcomes.

Thirdly, an important limitation of this study is that it was not powered to detect a difference in FtF psychotherapy sessions, but short-term clinical effects. Powering the current trial to treatment sessions would have required 612 patients in both treatment arms. This is a recognised issue in cost-effectiveness analyses alongside clinical trials (Briggs, 2000), where it is often considered unethical to continue patient recruitment after including the number of patients needed to demonstrate a clinical effect. Moreover, because patient recruitment fell short of initially proposed numbers due to logistical challenges, statistical power was also insufficient to show a statistically significant difference in effects. As such, statistical power was also insufficient to perform subgroup analyses based on specific subgroups such as different types of phobias. However, most patients in this sample were diagnosed with more than one phobia (Kok et al., 2014), often from different phobia subtypes, and this would have made clustering into subgroups difficult.
A major strength of this study is that it is, to our knowledge, the first to examine the effects of Internet–based guided self–help for phobias specifically in an outpatient setting, including a representative sample of outpatients from a naturalistic setting, analogous to a similar study for major depression (Kolovos et al., 2016).

Secondly, this trial uses a relatively long follow–up period. Finally, the intervention in this study did not replace conventional FtF component but was offered during a waiting list period.

FUTURE DIRECTIONS

Based on the findings and experiences from this trial, we propose a number of future directions for research and practice. Embedding an intervention similar to the one evaluated in the current trial into the health system could improve adherence and thus further reduce FtF usage. This might be done by having the patient’s designated therapist guide the web–based intervention, thus integrating the web–based intervention in routine care. Additionally, factors that improve the adherence to this (and other interventions) should be explored as pathways to increased uptake and clinical effectiveness. A rapidly emerging paradigm in outpatient clinics is the ‘blended’ model, where just parts of the FtF therapy are replaced by online components.

However, in contrast to fully online interventions, little is known the actual benefits these blended interventions, which has only recently gained research interest (e.g., Kooistra et al., 2014), and there is some criticism as to the premature implementation of such blended intervention (Ruwaard & Kok, 2015). In sum, results from this trial can be beneficial to the emerging field of blended treatments as it shows tentative feasibility and cost data of adding online therapy to routine psychiatric outpatient care.

CONCLUSIONS

This study showed that there were no statistically significant differences in costs and effects after 12 months between a group receiving an Internet–based intervention followed by FtF psychotherapy for phobias when compared to
a usual waiting list condition followed by FtF psychotherapy. Although the intervention group appeared to use fewer sessions of FtF therapy, this difference was not statistically significant.

Based on the results, the intervention is not considered cost-effective in comparison with control. Future improvements are needed in terms of uptake of and adherence to the intervention. Offering web-based interventions as in the current study to motivated outpatients during waiting list may be beneficial to both patients and outpatient clinics, but more research is needed.

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