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Does internet-based cognitive behaviour therapy reduce healthcare costs and resource use in treatment of social anxiety disorder? A cost minimisation analysis conducted alongside a randomized controlled trial

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3 **Does internet-based cognitive behaviour therapy reduce healthcare costs and resource**
4 **use in treatment of social anxiety disorder? A cost minimisation analysis conducted**
5 **alongside a randomized controlled trial**
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Abstract

Objectives: Social anxiety disorder (SAD) can be effectively treated with internet-delivered cognitive behavioural therapy (ICBT), but studies on long-term cost-minimization from a healthcare provider perspective in comparison to an evidence-based control treatment of therapeutic equivalence are lacking. The objective of the study was to determine whether ICBT reduces healthcare costs and use of healthcare resources compared to cognitive behavioural group therapy (CBGT).

Design: A cost-minimization study alongside an RCT where participants (N=126) with a diagnosis SAD were randomised to ICBT or to CBGT. Costs measured from a healthcare provider perspective were estimated using time-driven activity based costing alongside with health status over four years from baseline measured with EQ-5D.

Setting: A psychiatric outpatient clinic in Stockholm, Sweden.

Participants: Participants were 126 individuals with social anxiety disorder.

Primary and secondary outcome measures: Changes in EQ-5D and costs.

Interventions: Participants received either cognitive behavioral group therapy (CBGT) or Internet-based cognitive behavior therapy (ICBT) ICBT for a duration of 15 weeks.

Results: ICBT minimized total treatment costs. Mean improvement in health status ($d = -0.36$ to -0.25) was equivalent in both treatments over the study period, while healthcare costs were

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3 lower in ICBT (463 €, 95% CI: 446 € to 480 €) compared with the control group (806 € (95%
4
5 CI: 730 € to 883 €). Mean use of effective psychologist time in ICBT was 189.60 (SD =
6
7 53.77) minutes compared to 499.78 (SD = 30.91) in the CBGT group.
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10
11 **Conclusions:** In treatment of SAD, ICBT is equally effective but is associated with more
12
13 efficient staff utilization and considerably less costs compared with CBGT. From a health
14
15 care provider perspective, ICBT is an advantageous treatment option.
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20 21 **Strengths and limitations of this study**

- 22 • Randomized controlled design.
- 23 • Low attrition rates.
- 24 • Includes long-term follow-up data.
- 25 • It may be difficult to generalize time and cost estimates of resource use to other
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32 settings.
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37 38 **<Introduction>**

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41 Common mental health problems including depression and anxiety disorders are a major
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43 concern globally, and in the UK affecting approximately 17% of the population (1). The cost
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45 of these problems in England alone has been estimated at £105.2 billion (approximately 121
46
47 billion Euros) which includes costs associated with reduced health-related quality of life, lost
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49 productivity and social and health care costs (2). Social anxiety disorder (SAD) is one of the
50
51 most prevalent anxiety disorders with a 12-month prevalence of 2.8%-7.1% and a lifetime
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53 prevalence of 5%-12.1% (3-5). SAD is associated with functional impairment and typically
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55 follows a chronic course if untreated (6-9). The National Institute for Health and Care
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3 Excellence (NICE) in the UK recommends cognitive behavioural therapy (CBT) as the first-
4 line treatment option for SAD (10). Cognitive behavioural group therapy (CBGT) is an
5 effective format of CBT provision in the treatment of SAD (11, 12). Although patients prefer
6 psychological therapies to medication, access is limited in both primary and secondary care.
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12 (13)

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14 Recently, Internet-based cognitive behaviour therapy (ICBT) has emerged as an
15 empirically supported treatment for SAD with effect sizes on par with those of CBGT and
16 tested in at least 16 randomized controlled trials (14). Even though some previous studies
17 indicate that ICBT for SAD can be cost-effective (15, 16), evidence is lacking concerning
18 health economic evaluations from a health care provider perspective. In the present study we
19 used the time-driven activity based costing method, which is a method that takes into account
20 all costs related to the treatment from the health care provider's perspective. To our
21 knowledge, this has not been previously done concerning ICBT for SAD.
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32 The difference between cost-effectiveness analysis (CEA) and cost-
33 minimization analysis (CMA) has been discussed elsewhere (17); a full cost-effectiveness
34 analysis is often a preferred method to assess differences in both costs and effects. However,
35 in the context of a non-inferiority trial where treatments have been found to be equally
36 effective, CMA may be an appropriate method to analyze cost differences (18), since the
37 focus of interest is which treatment is less expensive.
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45 The original RCT demonstrated that both treatment delivery methods yielded
46 similar health improvements. In the present study, given the equivalence in treatment
47 effectiveness, the aim was to assess whether ICBT would help minimize the costs of
48 healthcare use relative to CBGT by using both data from a randomized controlled trial (19)
49 and additionally collected data on resource use. In contrast to previous health economic
50 evaluations (15, 20), the present study adopted a health care provider perspective using time-
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3 driven activity based costing methodology. If ICBT is found to help minimize the costs of
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5 healthcare use relative to CBGT, such internet-based interventions have the potential to
6
7 increase access to psychological therapy in psychiatry and primary care and could represent
8
9 an efficient alternative psychological treatment for SAD.
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11 12 13 <Method>

14 15 <Design>

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17 This was a cost-minimization analysis adopting a healthcare provider perspective, conducted
18
19 alongside a non-inferiority trial within the context of a parallel group study with unrestricted
20
21 randomization in 1:1 ratio (ICBT or CBGT). Costs measured from a healthcare provider
22
23 perspective were estimated using time-driven activity based costing alongside with health
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25 status over four years from baseline measured with EQ-5D. All costs were estimated based on
26
27 thorough assessment of the costs associated with ICBT when delivered in regular care (which
28
29 was implemented at the clinic after the RCT); this was done in order not to underestimate the
30
31 treatment costs. The trial was registered at clinicaltrials.gov (identifier NCT00564967). The
32
33 main outcome study has been reported elsewhere (19).
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40 41 <Recruitment, inclusion criteria and participants>

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43 The study was conducted at a public ICBT unit in Stockholm, Sweden (Stockholm Health
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45 Care Services). Participants were recruited by self-referral (n = 97) or by referral from
46
47 primary care physicians and psychiatrists (n = 29). The study protocol was approved by the
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49 Regional Ethical Review Board in Stockholm and informed consent was obtained from all
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51 participants. The recruitment took place between 2007 and 2009. The participant flow
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53 throughout the trial is presented in the main outcome study (19).
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3 <Treatments>
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5 ≤ Internet-based cognitive behaviour therapy (ICBT)>
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7 The internet-delivered treatment was based on and adapted from a treatment originally
8 developed by Andersson and colleagues and followed a CBT model developed for individual
9 therapy of SAD (21-23). The treatment content was accessed as text modules similar to
10 chapters in self-help bibliotherapy. Each chapter corresponded to a CBT session with a
11 specific theme such as cognitive restructuring, graded exposure or behavioral experiments,
12 coupled with homework assignments. Patients received supportive email feedback from a
13 psychologist after each module. The duration of the internet-based intervention was 15 weeks,
14 and therapists were instructed to restrict time spent on each patient to approximately 10
15 minutes per week.
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29 ≤ Cognitive behavioural group therapy (CBGT)>
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31 The group CBT for SAD followed the protocol developed by Heimberg and Becker (2002).
32 The treatment was equally long as the ICBT (i.e. 15 weeks) consisting of one initial
33 individual session followed by 14 group sessions. Each session was 2.5 hours long and led by
34 therapists trained in CBT. Each group consisted of six to seven patients.
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43 <Outcome measure>
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45 EuroQol (EQ-5D) index values were used to assess improvements in health-related quality of
46 life (EuroQol-Group, 1990). The EQ-5D is non-disease specific and measures five health
47 domains of importance to quality of life: mobility, self-care, usual activities, pain/discomfort
48 and anxiety/depression.
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55 <Resource use>
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3 Resource use was estimated by using a bottom-up approach where the clinical and
4
5 administrative activities performed throughout the treatment delivery cycle were first
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7 documented through process maps. This allowed us to identify resource use in terms of type
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9 (e.g. personnel, hospital space, IT) and time (measured in minutes and collected through time
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11 studies and interviews). The time studies and estimations on resource use were conducted at
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13 the treatment facility after the original RCT had been completed, i.e. when the treatment had
14
15 been implemented as routine care.
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18 19 20 <Costs> 21

22 Time-driven activity-based costing (TDABC) was used to determine the costs associated with
23
24 ICBT and CBGT from a healthcare provider perspective (24). Based on estimated resource
25
26 use (described above), the capacity cost rate (i.e. cost per minute) was calculated for each
27
28 resource. For example, the minute-cost for a psychologist was calculated by dividing the total
29
30 annual salary by the total number of minutes worked. Since not all time worked was available
31
32 for clinical care due to meetings, training and breaks etc., the practical capacity of each staff
33
34 category was estimated to be 80% of the actual number of worked hours, which is typically
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36 used as a standard assumption (24). Finally, the total cost of each treatment episode was
37
38 calculated for each patient by multiplying the minute cost for each resource with the total
39
40 number of minutes spent on each activity and then summing across all resources. Time
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42 estimates (and thus costs) not related to psychologists (e.g. assessments by medical doctors
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44 and administrative tasks by nurses and secretaries outside of treatment) were assumed to be
45
46 similar in both groups. Costs and were discounted at an annual rate of 5% and are presented in
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48 € , year 2017 values.
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53 54 55 <Cost-minimization analysis> 56 57 58 59 60

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3 Since previous studies have demonstrated equivalence in treatment effectiveness, a CMA was
4 conducted where costs per course of treatment from a healthcare provider perspective were
5 calculated and compared between treatment groups in a cost-minimization analysis; if total
6 costs were reduced by more efficient resource use, cost-minimization may be achieved (18).
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8 In order to avoid biased estimation of uncertainty, we have used the statistical methods of
9 cost-effectiveness to evaluate the joint distributions of costs and benefits.
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19 <Results>

20 <Outcomes>

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22 As previously reported (20) the between-group effect size on EQ5D was -0.18 (95% CI: -0.53
23 to 0.17), indicating equivalence in treatment effects. The within-group effect size was -0.36
24 (95% CI: -0.70 to -0.01) for ICBT and -0.25 (95% CI: -0.60 to 0.10) for CBGT.
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32 <Resource use>

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34 An independent-samples t-test was conducted to compare psychologist time in ICBT and
35 CBGT treatments. There was a significantly lower use of psychologist time in ICBT (M =
36 189.60, SD = 53.77) compared to CBGT (M = 499.78, SD = 30.91), with a mean difference
37 of 310.16 (95% CI: 248.47 to 371.86) minutes; $t(124) = 9.95, p < .001$. Table 1 presents
38 average number of minutes consumed per resource category over a complete cycle of care.
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47 INSERT TABLE 1 ABOUT HERE.
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51 <Costs and cost-minimization>

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53 Mean total healthcare costs are reported in Table 1. Taking into account the complete
54 treatment episode, total estimated cost for ICBT was 463 € (95% CI: 446 € to 480 €) per
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3 patient compared with 806 € (95% CI: 730 € to 883 €) for CBGT. Table 1 also presents the
4
5 average costs for each resource involved in the complete care episode, where costs of hospital
6
7 space, supervision, IT and management has been allocated over each staff category. Estimated
8
9 capacity cost rates (cost per minute) were 1.21 €/min for coordinating nurses, 1.02 €/min for
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11 medical secretaries, 1.24 €/min for psychologists, 1.40 €/min for resident physicians and 2.13
12
13 €/min for psychiatrists.
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16 The estimated cost-saving of ICBT relative to CBGT was -343 € (95% CI: -267
17
18 € to -420 €). Confidence-ellipses around the point estimate are showed in Fig. 1. As the 95%
19
20 and 75% confidence ellipses occupy both the south-east (SE) and south-west (SW) quadrants,
21
22 this indicates that the ICBT treatment was equally effective but less costly relative to the
23
24 CBGT intervention; the entire density within the ellipses involves cost-savings.
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30 INSERT FIG. 1 ABOUT HERE
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33 34 <Discussion>

35 36 < Principal findings >

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38 The objective of this study was to assess whether ICBT is less costly relative to CBGT in the
39
40 treatment of patients with SAD. While clinical treatment effects were equivalent, healthcare
41
42 costs were lower in the ICBT group (463 €) compared with the CBGT group (806 €). This
43
44 study thus showed that ICBT for SAD is clearly less costly compared to CBGT from a health
45
46 care provider perspective. These results add to the previous body of research demonstrating
47
48 that ICBT is associated with improved economic outcomes. (25) However, most health
49
50 economic evaluations have mainly been performed from a societal perspective. By using a
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52 healthcare provider perspective, and a TDABC costing approach, this study may help to
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3 develop a greater understanding of the costs incurred by the resources used throughout the
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5 clinical care of patients and by their administrative processes.
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10 *<Implications for policy and practice>*

11 Evidence suggests that ICBT is equally effective as the more commonly provided face-to-face
12 CBT, not only for SAD (19, 26) but for a wide range of mood and anxiety disorders (27),
13 while requiring less healthcare resources. Therefore, ICBT may have a number of advantages
14 that would benefit both health care providers and patients. First, since ICBT requires
15 significantly less therapist time, each therapist is able to treat more patients simultaneously,
16 consequentially increasing treatment availability and shortening waiting lists. Another
17 advantage is that ICBT overcomes geographic barriers for patients and thus to provide access
18 to evidence based psychological treatment at more equal opportunities. Finally, accessing
19 therapy sessions online is practical and more economical for patients because it enables them
20 to work with the treatment at their own convenience, and not having to take time off work for
21 making visits to their healthcare provider. To further increase access to evidence based
22 psychological interventions for SAD, ICBT may be considered as an alternative to face-to-
23 face psychological therapies as an initial step within a stepped care approach. This should also
24 be considered for other evidence based ICBT applications such as in depression and panic
25 disorder.
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47 *<Strengths and limitations>*

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49 The main strengths of the present study were the randomized controlled design, the direct
50 comparison of ICBT against face-to-face CBT, and the low attrition rates. However, the study
51 had some limitations.
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3 First, the use of TDABC as a costing methodology in healthcare is relatively
4 new, particularly within mental health care; it has been more commonly used in industry. (28-
5 30) Therefore, its validity may be difficult to evaluate at this stage. Also, although CBT
6 treatment delivery may be similar across different healthcare providers, supporting
7 administrative processes and clinical practices might differ significantly. As a result, it may
8 be difficult to generalize time and cost estimates of the total healthcare episode to other
9 settings and healthcare providers.
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18 A second limitation relates to difficulties in arriving at accurate time estimates
19 of resource use and activities performed. Since actual logging of time requires an electronic
20 measurement system, only accurate timing of the amount of time each psychologist spent with
21 each patient in ICBT could be recorded (thus providing measures of variability), whereas
22 other clinical and administrative processes were based on estimated average standard times.
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29 Third, parts of the time studies and estimations on resource use were carried out
30 several years after the original RCT, i.e. when the treatment had been implemented as routine
31 care. Although administrative routines and processes have remained more or less similar over
32 the years, there may still be differences when compared to how the administrative processes
33 were during the RCT.
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40 Finally, we will comment on the choice of cost-minimization analysis in the
41 present study. Economic evaluations in healthcare compare treatment options or technologies
42 in terms of clinical effects and costs, typically resulting in a cost-effectiveness ratio. The
43 incremental cost-effectiveness ratio (ICER) summarises the cost-effectiveness of a treatment
44 relative to an alternative by calculating the difference in costs between the two divided by the
45 difference in effects (18). We have previously estimated an ICER from a societal perspective
46 using the formula $(C_{ICBT} - C_{CBGT}) / (E_{ICBT} - E_{CBGT})$, where C_{ICBT} and E_{ICBT} represents the cost
47 and effect in the ICBT group and where C_{CBGT} and E_{CBGT} represent the cost and effect in the
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3 CBGT group (15, 20). Since both treatments were found to have equivalent efficacy,
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5 estimating an ICER may not be the optimal approach in this study as the ICER approaches
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7 infinity when effect difference is close to zero. However, if ICBT can reduce resource use in
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9 treatment of SAD, it may lower healthcare costs. Therefore, a cost-minimization approach
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11 was considered more appropriate in this study.
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16 <Conclusion>
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18 In treatment of SAD, ICBT is equally effective but is associated with more efficient staff
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20 utilization and considerably lower costs compared with CBGT. From a health care provider
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22 perspective, ICBT is an advantageous treatment option.
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5 **Contributions of authors:** SAE designed the study, performed the analyses, collected and
6
7 interpreted the data and drafted the paper. EH designed the study, developed the treatment,
8
9 performed the analyses, and drafted the paper. NL designed the study, interpreted the data,
10
11 and drafted the paper.
12
13

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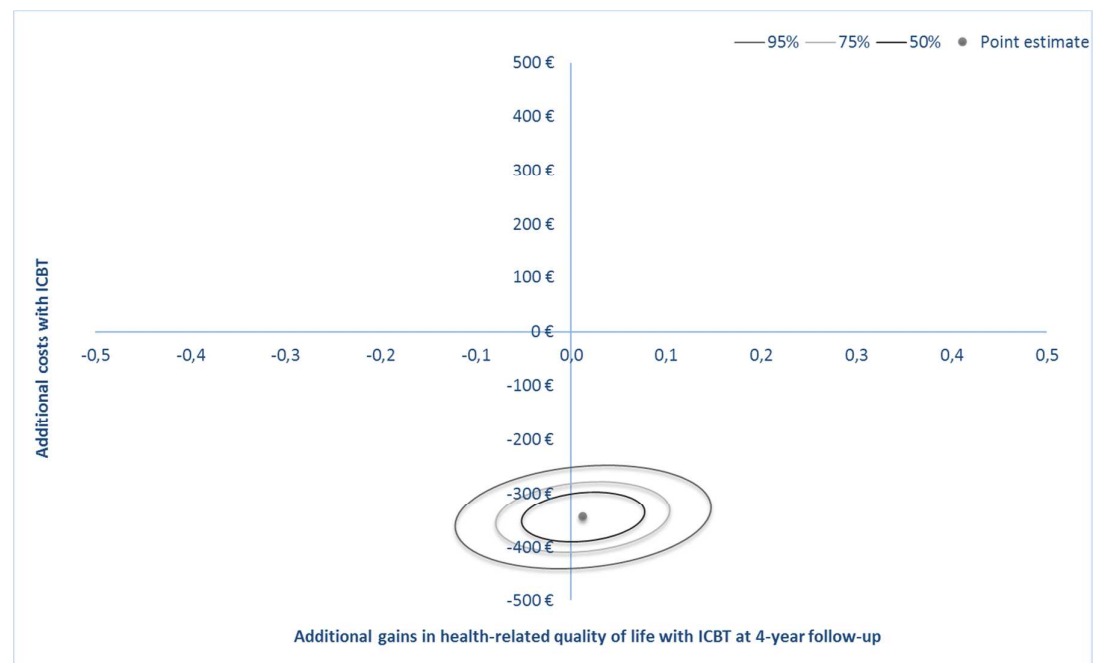
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37
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43 **Competing interests:** None declared.
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48 **Data sharing statement:** No additional data are available.
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Fig. 1. Mean differences in costs and gained health-related quality of life



Note. Each confidence-ellipse represents regions with a 50%, 75% or 95% probability of containing the true difference in cost and effect. Abbreviations: ICBT, internet-based cognitive behaviour therapy;

Tables

Table 1. Estimation of a patient's cost over a complete cycle of care for treating social anxiety disorder with ICBT or with CBGT

| | Coordinating nurse | | Psychiatrist | | Resident physician | | Psychologist | | Medical secretary | | Total | |
|--|--------------------|--------------|-----------------|--------------|--------------------|--------------|-----------------|--------------|-------------------|--------------|-----------------|--------------|
| | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost |
| ICBT | | | | | | | | | | | | |
| Registration and Verification | 11 | 13€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 11 | 13€ |
| Diagnostic assessment | 0 | 0€ | 20 | 43€ | 80 | 112€ | 0 | 0€ | 0 | 0€ | 100 | 154€ |
| Supervision meeting / discussion | 0 | 0€ | 3 | 6€ | 3 | 4€ | 1 | 1€ | 0 | 0€ | 7 | 11€ |
| Supplementary psychological assessment | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 7€ | 0 | 0€ | 5 | 7€ |
| Administrating treatment activation | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 41 | 41€ | 41 | 41€ |
| ICBT intervention (online) | 0 | 0€ | 0 | 0€ | 0 | 0€ | 82 | 102€ | 0 | 0€ | 82 | 102€ |
| ICBT intervention (offline) | 0 | 0€ | 0 | 0€ | 0 | 0€ | 77 | 95€ | 0 | 0€ | 77 | 95€ |
| Administrative preparation for follow-up visit | 3 | 3€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 3 | 3€ |
| Post-treatment clinical visit | 0 | 0€ | 0 | 0€ | 0 | 0€ | 24 | 30€ | 0 | 0€ | 24 | 30€ |
| Discharge | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 5€ | 5 | 5€ |
| Total | 14 | 17€ | 23 | 49€ | 83 | 116€ | 190 | 235€ | 46 | 46€ | 355 | 463€ |
| CBGT | | | | | | | | | | | | |
| Registration and Verification | 11 | 13€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 11 | 13€ |
| Diagnostic assessment | 0 | 0€ | 20 | 43€ | 80 | 112€ | 0 | 0€ | 0 | 0€ | 100 | 154€ |
| Supervision meeting / discussion | 0 | 0€ | 3 | 6€ | 3 | 4€ | 1 | 1€ | 0 | 0€ | 7 | 11€ |
| Supplementary psychological assessment | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 7€ | 0 | 0€ | 5 | 7€ |

| | | | | | | | | | | | | |
|--|-----------|------------|-----------|------------|-----------|-------------|------------|-------------|----------|-----------|------------|-------------|
| CBGT intervention | 0 | 0€ | 0 | 0€ | 0 | 0€ | 470 | 582€ | 0 | 0€ | 470 | 582€ |
| Administrative preparation for follow-up visit | 3 | 3€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 3 | 3€ |
| Post-treatment clinical visit | 0 | 0€ | 0 | 0€ | 0 | 0€ | 24 | 30€ | 0 | 0€ | 24 | 30€ |
| Discharge | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 5€ | 5 | 5€ |
| Total | 14 | 17€ | 23 | 49€ | 83 | 116€ | 500 | 619€ | 5 | 5€ | 625 | 806€ |

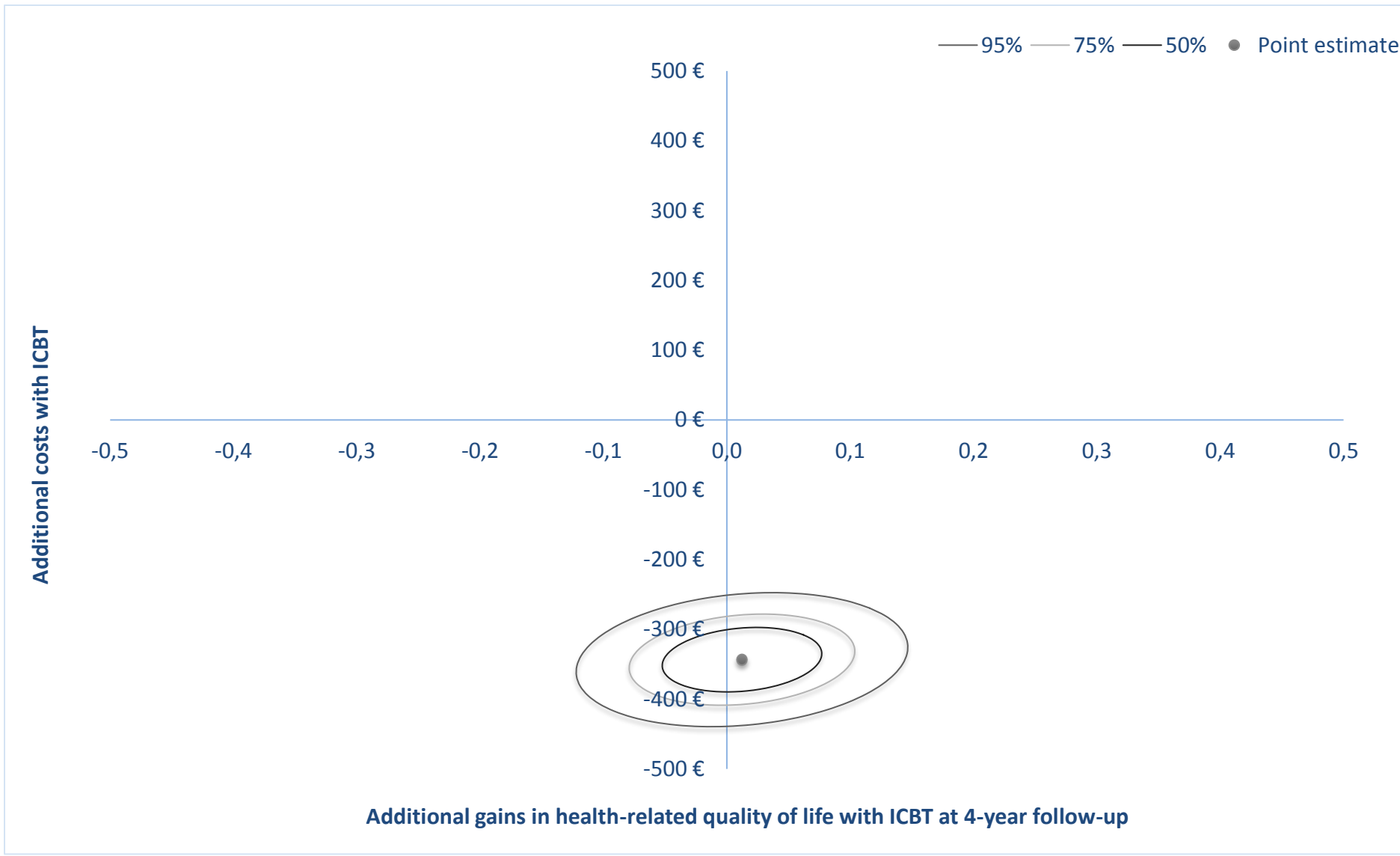
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HEALTH ECONOMIC EVALUATION OF ICBT FOR SAD

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CHEERS checklist—Items to include when reporting economic evaluations of health interventions

| Section/item | Item No | Recommendation | Reported on page No/ line No |
|--|---------|--|-----------------------------------|
| Title and abstract | | | |
| Title | 1 | Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared. | page 1, line 2 |
| Abstract | 2 | Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions. | page 2, line 1 to 24 |
| Introduction | | | |
| Background and objectives | 3 | Provide an explicit statement of the broader context for the study. | page 3, line 7 to page 4, line 18 |
| | | Present the study question and its relevance for health policy or practice decisions. | page 4, line 9 to 18 |
| Methods | | | |
| Target population and subgroups | 4 | Describe characteristics of the base case population and subgroups analysed, including why they were chosen. | page 4, line 20 and continued. |
| Setting and location | 5 | State relevant aspects of the system(s) in which the decision(s) need(s) to be made. | page 4, line 20 and continued. |
| Study perspective | 6 | Describe the perspective of the study and relate this to the costs being evaluated. | page 6, line 21 and continued. |
| Comparators | 7 | Describe the interventions or strategies being compared and state why they were chosen. | page 4, line 20 and continued |
| Time horizon | 8 | State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate. | page 5, line 1 |
| Discount rate | 9 | Report the choice of discount rate(s) used for costs and outcomes and say why appropriate. | page 7, line 11 |
| Choice of health outcomes | 10 | Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed. | page 6, line 9 |
| Measurement of effectiveness | 11a | <i>Single study-based estimates</i> : Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data. | page 7, line 24 |
| | 11b | <i>Synthesis-based estimates</i> : Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data. | |
| Measurement and valuation of preference based outcomes | 12 | If applicable, describe the population and methods used to elicit preferences for outcomes. | not applicable |
| Estimating resources and costs | 13a | <i>Single study-based economic evaluation</i> : Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | |

| Section/item | Item No | Recommendation | Reported on page No/ line No |
|--|---------|---|---------------------------------------|
| | 13b | <i>Model-based economic evaluation:</i> Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | not applicable |
| Currency, price date, and conversion | 14 | Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate. | page 7, line 12 |
| Choice of model | 15 | Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended. | page 7, line 14 |
| Assumptions | 16 | Describe all structural or other assumptions underpinning the decision-analytical model. | |
| Analytical methods | 17 | Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty. | page 7, line 19 |
| Results | | | |
| Study parameters | 18 | Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended. | page 8, lines 11 to 24 |
| Incremental costs and outcomes | 19 | For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios. | figure 1; page 8, lines 11 to 24 |
| Characterising uncertainty | 20a | <i>Single study-based economic evaluation:</i> Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective). | figure 1 |
| | 20b | <i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions. | not applicable |
| Characterising heterogeneity | 21 | If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information. | not applicable |
| Discussion | | | |
| Study findings, limitations, generalisability, and current knowledge | 22 | Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge. | page 9, line 3 to page 11, line 21 |

| Section/item | Item No | Recommendation | Reported on page No/ line No |
|-----------------------|---------|---|--|
| Other | | | |
| Source of funding | 23 | Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support. | page 12, line 16 |
| Conflicts of interest | 24 | Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations. | Information provided via the submission system |

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist

BMJ Open

Does internet-based cognitive behaviour therapy reduce healthcare costs and resource use in treatment of social anxiety disorder? A cost- minimisation analysis conducted alongside a randomized controlled trial

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| Secondary Subject Heading: | Health economics |
| Keywords: | MENTAL HEALTH, PSYCHIATRY, Anxiety disorders < PSYCHIATRY |
| | |

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3 **Does internet-based cognitive behaviour therapy reduce healthcare costs and resource**
4 **use in treatment of social anxiety disorder? A cost-minimisation analysis conducted**
5 **alongside a randomized controlled trial**
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14 Samir El Alaoui, PhD; Erik Hedman, PhD, Brjánn Ljótsson, PhD, and Nils Lindefors, MD,
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49 Figures: 3
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Abstract

Objectives: Social anxiety disorder (SAD) can be effectively treated with internet-delivered cognitive behavioural therapy (ICBT), but studies on long-term cost-minimisation from a healthcare provider perspective in comparison to an evidence-based control treatment of therapeutic equivalence are lacking. The objective of the study was to determine whether ICBT reduces healthcare costs and use of healthcare resources compared to cognitive behavioural group therapy (CBGT).

Design: A cost-minimisation study alongside an RCT where participants (N=126) with SAD were randomised to ICBT or to CBGT. Costs measured from a healthcare provider perspective were estimated using time-driven activity based costing alongside health status over four years from baseline measured with EQ-5D.

Setting: A psychiatric outpatient clinic in Stockholm, Sweden.

Participants: Participants were 126 individuals with social anxiety disorder.

Primary outcome measures: Changes in EQ-5D and costs.

Interventions: Participants received either CBGT or ICBT for a duration of 15 weeks.

Results: ICBT minimized total treatment costs. Mean improvement in health status ($d = -0.36$ to -0.25) was equivalent in both treatments over the study period, while healthcare costs were lower in ICBT (463 €, 95% CI: 446 € to 480 €) compared with CBGT (806 € (95% CI: 730 €

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3 to 883 €). Mean use of effective psychologist time in ICBT was 189.60 (SD = 53.77) minutes
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5 compared to 499.78 (SD = 30.91) in the CBGT group.
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10 **Conclusions:** In treatment of SAD, ICBT is equally effective but is associated with more
11 efficient staff utilization and less costs compared with CBGT. From a health care provider
12 perspective, ICBT is an advantageous treatment option.
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15 16 17 18 **Strengths and limitations of this study** 19

- 20 • Randomized controlled design.
- 21 • Low attrition rates.
- 22 • Includes long-term follow-up data.
- 23 • It may be difficult to generalize time and cost estimates of resource use to other
24 settings.
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34 **<Introduction>** 35 36 37

38 Common mental health problems including depression and anxiety disorders are a major
39 concern globally, and in the UK affecting approximately 17% of the population (1). The cost
40 of these problems in England alone has been estimated at £105.2 billion (approximately 121
41 billion Euros) which includes costs associated with reduced health-related quality of life, lost
42 productivity and social and health care costs (2). Social anxiety disorder (SAD) is one of the
43 most prevalent anxiety disorders with a 12-month prevalence of 2.8%-7.1% and a lifetime
44 prevalence of 5%-12.1% (3-5). SAD is associated with functional impairment and typically
45 follows a chronic course if untreated (6-9). The National Institute for Health and Care
46 Excellence (NICE) in the UK recommends cognitive behavioural therapy (CBT) as the first-
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3 line treatment option for SAD (10). Cognitive behavioural group therapy (CBGT) is an
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5 effective format of CBT provision in the treatment of SAD (11, 12). Although many patients
6
7 prefer psychological therapies to medication, access is limited in both primary and secondary
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9 care (13).
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12 Recently, Internet-based cognitive behaviour therapy (ICBT) has emerged as an
13
14 empirically supported treatment for SAD with effect sizes on par with those of CBGT and
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16 tested in at least 16 randomized controlled trials (14). Our research group has previously
17
18 compared ICBT to CBGT in a non-inferiority trial and found ICBT to be at least as effective
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20 as CBGT (15). At post-treatment, it was observed that 55% (95% CI, 42.5%–66.9%) of
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22 patients having received ICBT were classified as responders, compared to 34% (95% CI,
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24 22.1%–45.7%) having received CBGT. At six-month follow-up, the corresponding numbers
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26 were 64% (95% CI, 52.3%–75.8%) in the ICBT group and 45% (95% CI, 32.8%–57.6%) in
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28 the CBGT group.
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32 Even though some previous studies indicate that ICBT for SAD can be cost-
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34 effective (16, 17), evidence is lacking concerning health economic evaluations from a health
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36 care provider perspective. In the present study, we used the time-driven activity based costing
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38 method, which takes into account all costs related to the treatment from the health care
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40 provider's perspective. To our knowledge, this has not been previously done when evaluating
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42 ICBT for SAD.
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46 In health economic evaluations, a choice is often made between four types of
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48 methods: a cost-benefit analysis (CBA) in which both benefits and costs are expressed in
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50 monetary terms; a cost-effectiveness analysis (CEA) where costs and treatment effects are
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52 compared; a cost-utility analysis which is similar to CBA and CEA but where benefits is
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54 expressed in terms of quality-adjusted life years (QALYs); and finally, cost-minimisation
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3 analysis (CMA), which focuses on comparing the costs of different treatments with
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5 previously demonstrated equivalence in clinical efficacy.
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8 Given the equivalence of both treatment formats in terms of health
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10 improvements previously demonstrated in a randomized controlled trial (15), the purpose of
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12 this study was to assess whether ICBT may help minimize the costs of healthcare use relative
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14 to CBGT. This was done by using both data from a randomized controlled trial and
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16 additionally collected data on resource use. In contrast to previous health economic
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18 evaluations (16, 18), the present study adopted a health care provider perspective using time-
19
20 driven activity based costing (TDABC) methodology. If ICBT is found to help minimize the
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22 costs of healthcare use relative to CBGT, such internet-based interventions have the potential
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24 to increase access to psychological therapy in psychiatry and primary care and could represent
25
26 an efficient alternative psychological treatment for SAD.
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31 32 <Method>

33 34 <Design>

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36 This was a cost-minimisation analysis adopting a healthcare provider perspective, conducted
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38 alongside a non-inferiority trial within the context of a parallel group study with unrestricted
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40 randomization in 1:1 ratio (ICBT or CBGT). Costs measured from a healthcare provider
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42 perspective were estimated using time-driven activity based costing alongside with health
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44 status over four years from baseline measured with EQ-5D. All costs were estimated based on
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46 thorough assessment of the costs associated with ICBT when delivered in regular care (which
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48 was implemented at the clinic after the RCT); this was done in order not to underestimate the
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50 treatment costs. The trial was registered at clinicaltrials.gov (identifier NCT00564967). The
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52 main outcome study has been reported elsewhere (15).
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3 <Recruitment, inclusion criteria and participants>
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5 The study was conducted at a public ICBT unit in Stockholm, Sweden (Stockholm Health
6 Care Services). Participants were recruited by self-referral (n = 97) or by referral from
7 primary care physicians and psychiatrists (n = 29). The study protocol was approved by the
8 Regional Ethical Review Board in Stockholm and informed consent was obtained from all
9 participants. The recruitment took place between 2007 and 2009. The participant flow
10 throughout the trial is presented in the main outcome study (15).
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21 <Treatments>

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23 ≤ Internet-based cognitive behaviour therapy (ICBT)>

24 The internet-delivered treatment was based on and adapted from a treatment originally
25 developed by Andersson and colleagues and followed a CBT model developed for individual
26 therapy of SAD (19-21). The treatment content was accessed as text modules similar to
27 chapters in self-help bibliotherapy. Each chapter corresponded to a CBT session with a
28 specific theme such as cognitive restructuring, graded exposure or behavioral experiments,
29 coupled with homework assignments. Patients received supportive email feedback from a
30 psychologist after each module. The duration of the internet-based intervention was 15 weeks,
31 and therapists were instructed to restrict time spent on each patient to approximately 10
32 minutes per week.
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47 ≤ Cognitive behavioural group therapy (CBGT)>

48 The group CBT for SAD followed the protocol developed by Heimberg and Becker (2002).
49 The treatment was equally long as the ICBT (i.e. 15 weeks) consisting of one initial
50 individual session followed by 14 group sessions. Each session was 2.5 hours long and led by
51 therapists trained in CBT. Each group consisted of six to seven patients.
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5 <Outcome measure>
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7 EuroQol (EQ-5D) index values were used to assess improvements in health-related quality of
8 life (EuroQol-Group, 1990). The EQ-5D is non-disease specific and measures five health
9 domains of importance to quality of life: mobility, self-care, usual activities, pain/discomfort
10 and anxiety/depression.
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18 <Resource use>
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20 Resource use was estimated by using a bottom-up approach where the clinical and
21 administrative activities performed throughout the treatment delivery cycle were first
22 documented through process maps. This allowed us to identify resource use in terms of type
23 (e.g. personnel, hospital space, IT) and time (measured in minutes and collected through time
24 studies and interviews). The time studies and estimations on resource use were conducted at
25 the treatment facility after the original RCT had been completed, i.e. when the treatment had
26 been implemented as routine care.
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38 <Costs>
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40 TDABC was used to determine the costs associated with ICBT and CBGT from a healthcare
41 provider perspective (22). Based on estimated resource use (described above), the capacity
42 cost rate (i.e. cost per minute) was calculated for each resource. The overall approach for
43 calculating capacity cost rates for each resource involved the allocating of costs such as
44 hospital space, supervision, IT (computers, email, services, etc.) and management evenly per
45 minute. Costs for hospital space were calculated as the square meter price divided by floor
46 space per staff category and joint surfaces were then allocated. Shared costs included
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3 management as well as shared unit administration. Finally, hospital costs for security and
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5 safety were also included.
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7 The minute-cost for a psychologist was calculated by dividing the total annual
8 salary by the total number of minutes worked. Since not all time worked was available for
9 clinical care due to meetings, training and breaks etc., the practical capacity of each staff
10 category was estimated to be 80% of the actual number of worked hours, which is typically
11 used as a standard assumption (22). Finally, the total cost of each treatment episode was
12 calculated for each patient by multiplying the minute cost for each resource with the total
13 number of minutes spent on each activity and then summing across all resources. Time
14 estimates (and thus costs) not related to psychologists (e.g. assessments by medical doctors
15 and administrative tasks by nurses and secretaries outside of treatment) were assumed to be
16 similar in both groups. In addition to calculating actual costs, costs were also estimated when
17 discounted at annual rates of 3% and 5% respectively, and presented in €, year 2017 values.
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34 <Cost-minimisation analysis>

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36 Since the main outcome study have demonstrated equivalence in treatment efficacy, we chose
37 to conduct a CMA where costs per course of treatment from a healthcare provider perspective
38 were calculated and compared between treatment groups; if total costs were reduced by more
39 efficient resource use, cost-minimisation may be achieved (23). In order to avoid biased
40 estimation of uncertainty, we have used the statistical methods of cost-effectiveness to
41 evaluate the joint distributions of costs and benefits.
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51 <Sensitivity analysis>

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53 A probability sensitivity analysis was performed to estimate the uncertainty surrounding the
54 cost-effectiveness ratios. Confidence ellipses at 50%, 75%, and 95% were calculated and
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3 cost-effectiveness acceptability curves (CEACs) were constructed to represent the uncertainty
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5 around the estimate (24) in accordance with recommended guidelines (25). Incremental net
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7 benefit (INB) was used to interpret the CEAC, where the slope of the net monetary benefits
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9 (NMB) curve represents the difference in effects between ICBT and CBGT.
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11 <Results>

12 <Outcomes>

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18 As previously reported (18) the between-group effect size on EQ5D was -0.18 (95% CI: -0.53
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20 to 0.17), indicating equivalence in treatment effects. The within-group effect size was -0.36
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22 (95% CI: -0.70 to -0.01) for ICBT and -0.25 (95% CI: -0.60 to 0.10) for CBGT. Treatment
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24 adherence was similar across treatment conditions; out of possible 15 sessions and modules
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26 respectively, mean number of attended sessions was 9.40 (SD = 4.87) in the CBGT group
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28 and 9.33 (SD = 4.95) in the ICBT group. As previously reported, number of attendet
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30 treatment sessions/completed modules was positively related to treatment outcome (26).
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36 <Resource use>

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38 An independent-samples t-test was conducted to compare psychologist time in ICBT and
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40 CBGT treatments. There was a significantly lower use of psychologist time in ICBT (M =
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42 189.60, SD = 53.77) compared to CBGT (M = 499.78, SD = 30.91), with a mean difference
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44 of 310.16 (95% CI: 248.47 to 371.86) minutes; $t(124) = 9.95, p < .001$. Table 1 presents
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46 average number of minutes consumed per resource category over a complete cycle of care.
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51 INSERT TABLE 1 ABOUT HERE.
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55 <Costs and cost-minimisation>

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3 Mean total healthcare costs are reported in Table 1. Taking into account the complete
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5 treatment episode, total estimated cost for ICBT was 463 € (95% CI: 446 € to 480 €) per
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7 patient compared with 806 € (95% CI: 730 € to 883 €) for CBGT. Table 1 also presents the
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9 average costs for each resource involved in the complete care episode, where costs of hospital
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11 space, supervision, IT and management has been allocated over each staff category. Estimated
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13 capacity cost rates (cost per minute) were 1.21 €/min for coordinating nurses, 1.02 €/min for
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15 medical secretaries, 1.24 €/min for psychologists, 1.40 €/min for resident physicians and 2.13
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17 €/min for psychiatrists.
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21 The estimated cost-saving of ICBT relative to CBGT was 343 € (95% CI: 267 €
22
23 to 420 €). Fig. 1 illustrates confidence-ellipses around the point estimate; as the 95% and 75%
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25 confidence ellipses occupy both the south-east (SE) and south-west (SW) quadrants, this
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27 indicates that the ICBT treatment was equally effective but less costly relative to the CBGT
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29 intervention; the entire density within the ellipses involves cost-savings. Table 2 presents
30
31 costs and mean differences when taking account of time, assuming 3% and 5% annual
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33 discount rates; when costs were discounted at 3%, the mean difference was 305 € (95% CI:
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35 237 € to 373 €) and 283 € (95% CI: 220 € to 345 €) at a 5% discount rate.
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38 INSERT TABLE 2 ABOUT HERE
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43 INSERT FIG. 1 ABOUT HERE
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47 The cost-effectiveness acceptability curve (CEAC) is presented in **Fig. 2**. The CEAC
48
49 indicates the probability that ICBT is cost-effective compared with CBGT for a given value of
50
51 the maximum willingness to pay (WTP) for a gained unit of health-related quality of life. As
52
53 can be seen, the probability for ICBT being cost-effective is high regardless of WTP.
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3 INSERT FIG. 2 ABOUT HERE
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7 A graphical representation of the net benefit is illustrated in Fig. 3. The uncertainty of the
8 value of the intervention gets larger as the WTP for the clinical outcome increases; this is
9 reflected in the increasing CI of the INB. The positive NMBs suggest that the intervention is
10 cost-effective at four year follow-up assessment.
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18 INSERT FIG. 3 ABOUT HERE
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22 <Discussion>

23 < Principal findings >

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26 The objective of this study was to assess whether ICBT is less costly relative to CBGT in the
27 treatment of patients with SAD. While clinical treatment effects were equivalent, healthcare
28 costs were lower in the ICBT group (463 €) compared with the CBGT group (806 €). This
29 study thus showed that ICBT for SAD is clearly less costly compared to CBGT from a health
30 care provider perspective. These results add to the previous body of research demonstrating
31 that ICBT is associated with improved economic outcomes. (27) However, most health
32 economic evaluations have mainly been performed from a societal perspective. By using a
33 healthcare provider perspective, and a TDABC costing approach, this study may help to
34 develop a greater understanding of the costs incurred by the resources used throughout the
35 clinical care of patients and by their administrative processes.
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51 <Implications for policy and practice>

52 Evidence suggests that ICBT is equally effective as the more commonly provided face-to-face
53 CBT, not only for SAD (15, 28) but for a wide range of mood and anxiety disorders (29),
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3 while requiring less healthcare resources. Therefore, ICBT may have a number of advantages
4
5 that would benefit both health care providers and patients. First, since ICBT requires
6
7 significantly less therapist time, each therapist is able to treat more patients simultaneously,
8
9 consequentially increasing treatment availability and shortening waiting lists. Another
10
11 advantage is that ICBT overcomes geographic barriers for patients and thus to provide access
12
13 to evidence based psychological treatment at more equal opportunities. Finally, accessing
14
15 therapy sessions online is practical and more economical for patients because it enables them
16
17 to work with the treatment at their own convenience, and not having to take time off work for
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19 making visits to their healthcare provider. To further increase access to evidence based
20
21 psychological interventions for SAD, ICBT may be considered as an alternative to face-to-
22
23 face psychological therapies as an initial step within a stepped care approach. This should also
24
25 be considered for other evidence based ICBT applications such as in depression and panic
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27 disorder.
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34 *<Strengths and limitations>*

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36 The main strengths of the present study were the randomized controlled design, the direct
37
38 comparison of ICBT against face-to-face CBT, and the low attrition rates. However, the study
39
40 had some limitations.
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43 First, the use of TDABC as a costing methodology in healthcare is relatively
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45 new, particularly within mental health care; it has been more commonly used in industry. (30-
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47 32) Therefore, its validity may be difficult to evaluate at this stage. Also, although CBT
48
49 treatment delivery may be similar across different healthcare providers, supporting
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51 administrative processes and clinical practices might differ significantly. As a result, it may
52
53 be difficult to generalize time and cost estimates of the total healthcare episode to other
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55 settings and healthcare providers.
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3 A second limitation relates to difficulties in arriving at accurate time estimates
4 of resource use and activities performed. Since actual logging of time requires an electronic
5 measurement system, only accurate timing of the amount of time each psychologist spent with
6 each patient in ICBT could be recorded (thus providing measures of variability), whereas
7 other clinical and administrative processes were based on estimated average standard times.
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14 Third, parts of the time studies and estimations on resource use were carried out
15 several years after the original RCT, i.e. when the treatment had been implemented as routine
16 care. Although administrative routines and processes have remained more or less similar over
17 the years, there may still be minor differences when compared to how the administrative
18 processes were during the RCT. As a consequence, difficulties in retrieving exact cost data
19 may add to the uncertainty around cost estimates.
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28 Finally, we will comment on the choice of cost-minimisation analysis in the
29 present study. Economic evaluations in healthcare compare treatment options or technologies
30 in terms of clinical effects and costs, typically resulting in a cost-effectiveness ratio. The
31 incremental cost-effectiveness ratio (ICER) summarises the cost-effectiveness of a treatment
32 relative to an alternative by calculating the difference in costs between the two divided by the
33 difference in effects (23). We have previously estimated an ICER from a societal perspective
34 using the formula $(C_{ICBT} - C_{CBGT}) / (E_{ICBT} - E_{CBGT})$, where C_{ICBT} and E_{ICBT} represents the cost
35 and effect in the ICBT group and where C_{CBGT} and E_{CBGT} represent the cost and effect in the
36 CBGT group (16, 18). The difference between cost-effectiveness analysis (CEA) and cost-
37 minimisation analysis (CMA) has been further discussed elsewhere (33); a full cost-
38 effectiveness analysis is often a preferred method to assess differences in both costs and
39 effects. However, in the context of a non-inferiority trial where treatments have been found to
40 be equally effective, CMA may be an appropriate method to analyze cost differences (23),
41 since the focus of interest is which treatment is less expensive. Since both treatments in this
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3 study were found to have equivalent efficacy, estimating an ICER may not be the optimal
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5 approach as the ICER approaches infinity when effect difference is close to zero. However, if
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7 ICBT can reduce resource use in treatment of SAD, it may lower healthcare costs. Therefore,
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9 a cost-minimisation approach was considered more appropriate in this case.
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14 <Conclusion>

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16 In treatment of SAD, ICBT is equally effective but is associated with more efficient staff
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18 utilization and considerably lower costs compared with CBGT. From a health care provider
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20 perspective, ICBT is an advantageous treatment option.
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5 **Contributions of authors:** SAE designed the study, performed the analyses, collected and
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7 interpreted the data and drafted the paper. EH designed the study, developed the SAD
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9 treatment, performed the analyses, and drafted the paper. NL and BL designed the study,
10
11 interpreted the data, and drafted the paper.
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39
40 none of which had any role in the design, execution or publication of the study.
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45 **Competing interests:** None declared.
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50 **Data sharing statement:** No additional data are available.
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3 **Fig. 1.** *Mean differences in costs and gained health-related quality of life.*
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7 Note. Each confidence-ellipse represents regions with a 50%, 75% or 95% certainty around
8 the mean difference in cost and effect. Abbreviations: ICBT, internet-based cognitive
9 behaviour therapy.
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15 **Fig. 2.** *Cost-effectiveness acceptability curve at 4-year follow.*
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18 Note. The cost-effectiveness acceptability curve shows the probability that ICBT is cost-
19 effective with changes in the amount that society is willing to pay for a unit increase in health
20 related quality of life, considering healthcare costs.
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27 **Fig. 3.** *Net monetary benefit curves and 95% confidence intervals at 4-year follow-up.*
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Tables

Table 1. Estimation of a patient's cost over a complete cycle of care for treating social anxiety disorder with ICBT or with CBGT

| | Coordinating nurse | | Psychiatrist | | Resident physician | | Psychologist | | Medical secretary | | Total | |
|--|--------------------|--------------|-----------------|--------------|--------------------|--------------|-----------------|--------------|-------------------|--------------|-----------------|--------------|
| | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost |
| ICBT | | | | | | | | | | | | |
| Registration and Verification | 11 | 13€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 11 | 13€ |
| Diagnostic assessment | 0 | 0€ | 20 | 43€ | 80 | 112€ | 0 | 0€ | 0 | 0€ | 100 | 154€ |
| Supervision meeting / discussion | 0 | 0€ | 3 | 6€ | 3 | 4€ | 1 | 1€ | 0 | 0€ | 7 | 11€ |
| Supplementary psychological assessment | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 7€ | 0 | 0€ | 5 | 7€ |
| Administrating treatment activation | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 41 | 41€ | 41 | 41€ |
| ICBT intervention (online) | 0 | 0€ | 0 | 0€ | 0 | 0€ | 82 | 102€ | 0 | 0€ | 82 | 102€ |
| ICBT intervention (offline) | 0 | 0€ | 0 | 0€ | 0 | 0€ | 77 | 95€ | 0 | 0€ | 77 | 95€ |
| Administrative preparation for follow-up visit | 3 | 3€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 3 | 3€ |
| Post-treatment clinical visit | 0 | 0€ | 0 | 0€ | 0 | 0€ | 24 | 30€ | 0 | 0€ | 24 | 30€ |
| Discharge | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 5€ | 5 | 5€ |
| Total | 14 | 17€ | 23 | 49€ | 83 | 116€ | 190 | 235€ | 46 | 46€ | 355 | 463€ |
| CBGT | | | | | | | | | | | | |
| Registration and Verification | 11 | 13€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 11 | 13€ |
| Diagnostic assessment | 0 | 0€ | 20 | 43€ | 80 | 112€ | 0 | 0€ | 0 | 0€ | 100 | 154€ |
| Supervision meeting / discussion | 0 | 0€ | 3 | 6€ | 3 | 4€ | 1 | 1€ | 0 | 0€ | 7 | 11€ |
| Supplementary psychological assessment | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 7€ | 0 | 0€ | 5 | 7€ |

| | | | | | | | | | | | | |
|--|-----------|------------|-----------|------------|-----------|-------------|------------|-------------|----------|-----------|------------|-------------|
| CBGT intervention | 0 | 0€ | 0 | 0€ | 0 | 0€ | 470 | 582€ | 0 | 0€ | 470 | 582€ |
| Administrative preparation for follow-up visit | 3 | 3€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 3 | 3€ |
| Post-treatment clinical visit | 0 | 0€ | 0 | 0€ | 0 | 0€ | 24 | 30€ | 0 | 0€ | 24 | 30€ |
| Discharge | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 5€ | 5 | 5€ |
| Total | 14 | 17€ | 23 | 49€ | 83 | 116€ | 500 | 619€ | 5 | 5€ | 625 | 806€ |

HEALTH ECONOMIC EVALUATION OF ICBT FOR SAD

Table 2. *Estimation of actual and discounted costs of care for treating social anxiety disorder with ICBT or with CBGT*

| | Group | N | Mean cost, € | SD | Mean difference, € | 95% Confidence Interval of the Difference | |
|--|-------|----|--------------|-----|--------------------|---|-----|
| Total costs, actual | CBGT | 62 | 806 | 302 | | | |
| | ICBT | 64 | 463 | 67 | 343 | 267 | 420 |
| Total costs, discounted at 3% per year | CBGT | 62 | 717 | 268 | | | |
| | ICBT | 64 | 411 | 59 | 305 | 237 | 373 |
| Total costs, discounted at 5% per year | CBGT | 62 | 663 | 248 | | | |
| | ICBT | 64 | 381 | 55 | 283 | 220 | 345 |

HEALTH ECONOMIC EVALUATION OF ICBT FOR SAD

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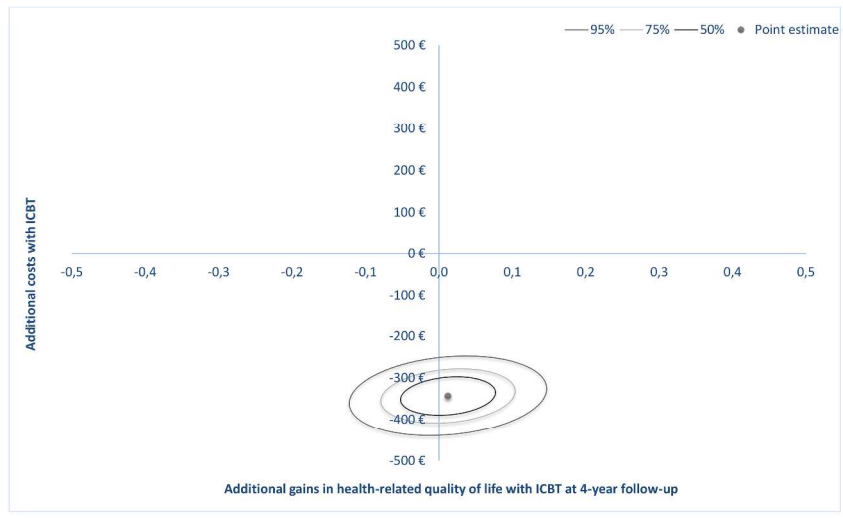


Fig. 1. Mean differences in costs and gained health-related quality of life.

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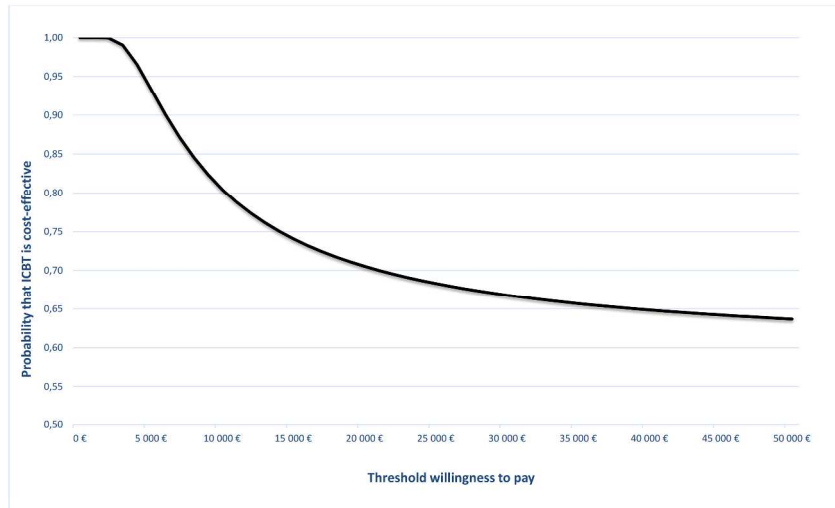


Fig. 2. Cost-effectiveness acceptability curve at 4-year follow.

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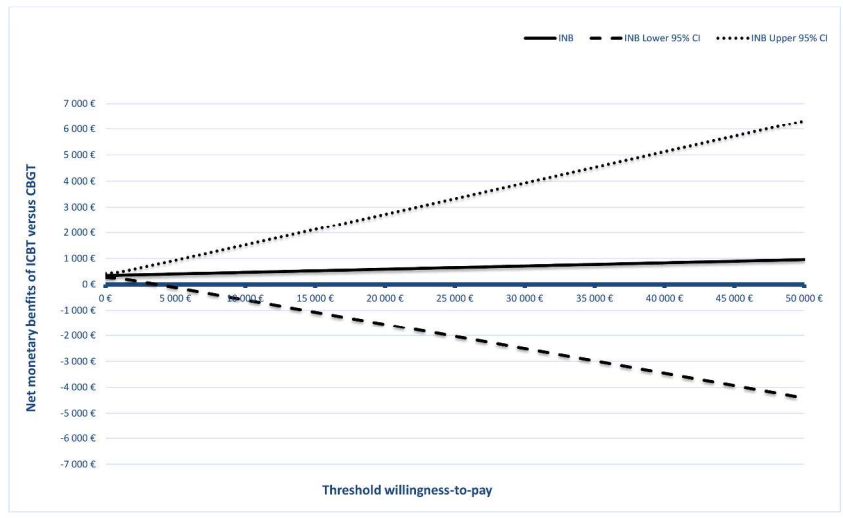


Fig. 3. Net monetary benefit curves and 95% confidence intervals at 4-year follow-up

297x210mm (300 x 300 DPI)

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| Control Group (CBGT) | | | Intervention Group (ICBT) | | |
|----------------------|--------|---------|---------------------------|--------|-------|
| Patient | Effect | Cost | Patient | Effect | Cost |
| 1 | ,12 | 1 091 € | 1 | ,56 | 546 € |
| 2 | -,54 | 223 € | 2 | ,13 | 389 € |
| 3 | -,89 | 595 € | 3 | -,04 | 453 € |
| 4 | ,19 | 1 153 € | 4 | -,59 | 482 € |
| 5 | ,15 | 1 153 € | 5 | ,15 | 495 € |
| 6 | ,00 | 1 091 € | 6 | -,54 | 364 € |
| 7 | -,04 | 1 153 € | 7 | -,43 | 503 € |
| 8 | ,40 | 905 € | 8 | ,15 | 457 € |
| 9 | ,08 | 347 € | 9 | ,08 | 403 € |
| 10 | ,15 | 409 € | 10 | ,04 | 476 € |
| 11 | ,08 | 843 € | 11 | ,56 | 557 € |
| 12 | ,15 | 223 € | 12 | ,00 | 519 € |
| 13 | ,54 | 781 € | 13 | ,15 | 473 € |
| 14 | ,03 | 905 € | 14 | ,00 | 447 € |
| 15 | ,31 | 781 € | 15 | ,08 | 493 € |
| 16 | ,08 | 1 029 € | 16 | ,15 | 397 € |
| 17 | ,19 | 1 091 € | 17 | ,28 | 447 € |
| 18 | ,20 | 1 091 € | 18 | ,28 | 399 € |
| 19 | -,47 | 347 € | 19 | ,51 | 437 € |
| 20 | ,43 | 595 € | 20 | ,28 | 379 € |
| 21 | ,19 | 1 029 € | 21 | ,28 | 499 € |
| 22 | ,08 | 967 € | 22 | ,31 | 483 € |
| 23 | ,05 | 1 091 € | 23 | ,28 | 406 € |
| 24 | -,86 | 595 € | 24 | ,08 | 575 € |
| 25 | ,20 | 1 091 € | 25 | ,28 | 530 € |
| 26 | ,20 | 223 € | 26 | ,43 | 508 € |
| 27 | ,15 | 1 091 € | 27 | -,43 | 469 € |
| 28 | ,13 | 719 € | 28 | ,00 | 490 € |
| 29 | ,77 | 285 € | 29 | ,08 | 621 € |
| 30 | ,20 | 595 € | 30 | ,08 | 385 € |
| 31 | ,12 | 1 153 € | 31 | -,08 | 394 € |
| 32 | ,08 | 223 € | 32 | ,00 | 416 € |
| 33 | ,40 | 1 091 € | 33 | -,27 | 384 € |
| 34 | ,51 | 967 € | 34 | ,08 | 477 € |
| 35 | -,43 | 781 € | 35 | ,15 | 410 € |
| 36 | ,28 | 905 € | 36 | ,03 | 431 € |
| 37 | ,00 | 285 € | 37 | ,08 | 507 € |
| 38 | ,15 | 1 091 € | 38 | ,00 | 522 € |
| 39 | -,82 | 223 € | 39 | ,28 | 502 € |
| 40 | ,15 | 657 € | 40 | ,12 | 468 € |
| 41 | ,08 | 595 € | 41 | -,07 | 372 € |
| 42 | ,24 | 1 091 € | 42 | ,15 | 385 € |
| 43 | ,43 | 657 € | 43 | -,01 | 534 € |
| 44 | ,20 | 967 € | 44 | -,54 | 377 € |
| 45 | ,00 | 967 € | 45 | ,28 | 429 € |
| 46 | -,10 | 1 153 € | 46 | ,19 | 428 € |

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|----|----|------|---------|----|------|-------|
| 1 | | | | | | |
| 2 | 47 | ,20 | 1 029 € | 47 | ,00 | 678 € |
| 3 | 48 | -,07 | 905 € | 48 | ,15 | 497 € |
| 4 | 49 | ,43 | 1 091 € | 49 | ,08 | 449 € |
| 5 | 50 | ,15 | 409 € | 50 | -,48 | 371 € |
| 6 | 51 | -,41 | 471 € | 51 | ,03 | 468 € |
| 7 | 52 | ,08 | 657 € | 52 | ,08 | 659 € |
| 8 | 53 | ,08 | 1 153 € | 53 | ,15 | 473 € |
| 9 | 54 | ,15 | 967 € | 54 | -,01 | 481 € |
| 10 | 55 | -,82 | 1 029 € | 55 | ,63 | 455 € |
| 11 | 56 | ,15 | 1 029 € | 56 | ,19 | 404 € |
| 12 | 57 | ,40 | 533 € | 57 | ,20 | 407 € |
| 13 | 58 | ,08 | 843 € | 58 | ,27 | 420 € |
| 14 | 59 | ,08 | 1 029 € | 59 | ,28 | 480 € |
| 15 | 60 | -,52 | 843 € | 60 | -,42 | 522 € |
| 16 | 61 | ,19 | 843 € | 61 | -,50 | 453 € |
| 17 | 62 | ,20 | 843 € | 62 | ,63 | 436 € |
| 18 | | | | 63 | -,07 | 400 € |
| 19 | | | | 64 | ,12 | 463 € |
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| 25 | | Mean | Mean | | Mean | Mean |
| 26 | | ,06 | 806 € | | ,08 | 463 € |
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CHEERS checklist—Items to include when reporting economic evaluations of health interventions

| Section/item | Item No | Recommendation | Reported on page No/ line No |
|--|---------|--|-----------------------------------|
| Title and abstract | | | |
| Title | 1 | Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared. | page 1, line 2 |
| Abstract | 2 | Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions. | page 2, line 1 to 24 |
| Introduction | | | |
| Background and objectives | 3 | Provide an explicit statement of the broader context for the study. | page 3, line 7 to page 4, line 18 |
| | | Present the study question and its relevance for health policy or practice decisions. | page 4, line 9 to 18 |
| Methods | | | |
| Target population and subgroups | 4 | Describe characteristics of the base case population and subgroups analysed, including why they were chosen. | page 4, line 20 and continued. |
| Setting and location | 5 | State relevant aspects of the system(s) in which the decision(s) need(s) to be made. | page 4, line 20 and continued. |
| Study perspective | 6 | Describe the perspective of the study and relate this to the costs being evaluated. | page 6, line 21 and continued. |
| Comparators | 7 | Describe the interventions or strategies being compared and state why they were chosen. | page 4, line 20 and continued |
| Time horizon | 8 | State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate. | page 5, line 1 |
| Discount rate | 9 | Report the choice of discount rate(s) used for costs and outcomes and say why appropriate. | page 7, line 11 |
| Choice of health outcomes | 10 | Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed. | page 6, line 9 |
| Measurement of effectiveness | 11a | <i>Single study-based estimates</i> : Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data. | page 7, line 24 |
| | 11b | <i>Synthesis-based estimates</i> : Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data. | |
| Measurement and valuation of preference based outcomes | 12 | If applicable, describe the population and methods used to elicit preferences for outcomes. | not applicable |
| Estimating resources and costs | 13a | <i>Single study-based economic evaluation</i> : Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | |

| Section/item | Item No | Recommendation | Reported on page No/ line No |
|--|---------|---|---------------------------------------|
| | 13b | <i>Model-based economic evaluation:</i> Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | not applicable |
| Currency, price date, and conversion | 14 | Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate. | page 7, line 12 |
| Choice of model | 15 | Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended. | page 7, line 14 |
| Assumptions | 16 | Describe all structural or other assumptions underpinning the decision-analytical model. | |
| Analytical methods | 17 | Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty. | page 7, line 19 |
| Results | | | |
| Study parameters | 18 | Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended. | page 8, lines 11 to 24 |
| Incremental costs and outcomes | 19 | For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios. | figure 1; page 8, lines 11 to 24 |
| Characterising uncertainty | 20a | <i>Single study-based economic evaluation:</i> Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective). | figure 1 |
| | 20b | <i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions. | not applicable |
| Characterising heterogeneity | 21 | If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information. | not applicable |
| Discussion | | | |
| Study findings, limitations, generalisability, and current knowledge | 22 | Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge. | page 9, line 3 to page 11, line 21 |

| Section/item | Item No | Recommendation | Reported on page No/ line No |
|-----------------------|---------|---|--|
| Other | | | |
| Source of funding | 23 | Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support. | page 12, line 16 |
| Conflicts of interest | 24 | Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations. | Information provided via the submission system |

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist

BMJ Open

Does internet-based cognitive behaviour therapy reduce healthcare costs and resource use in treatment of social anxiety disorder? A cost- minimisation analysis conducted alongside a randomized controlled trial

| | |
|---------------------------------|---|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2017-017053.R2 |
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| Primary Subject Heading: | Mental health |
| Secondary Subject Heading: | Health economics |
| Keywords: | PSYCHIATRY, Anxiety disorders < PSYCHIATRY, PUBLIC HEALTH |
| | |

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Manuscripts

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3 **Does internet-based cognitive behaviour therapy reduce healthcare costs and resource**
4 **use in treatment of social anxiety disorder? A cost-minimisation analysis conducted**
5 **alongside a randomized controlled trial**
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14 Samir El Alaoui, PhD; Erik Hedman, PhD, Brjánn Ljótsson, PhD, and Nils Lindefors, MD,
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45 Word count: 3414 (main text); 288 (abstract)
46

47 Tables: 5
48

49 Figures: 3
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Abstract

Objectives: Social anxiety disorder (SAD) can be effectively treated with internet-delivered cognitive behavioural therapy (ICBT), but studies on long-term cost-minimisation from a healthcare provider perspective in comparison to an evidence-based control treatment of therapeutic equivalence are lacking. The objective of the study was to determine whether ICBT reduces healthcare costs and use of healthcare resources compared to cognitive behavioural group therapy (CBGT).

Design: A cost-minimisation study alongside an RCT where participants (N=126) with SAD were randomised to ICBT or to CBGT. Costs measured from a healthcare provider perspective were estimated using time-driven activity based costing alongside health status over four years from baseline measured with EQ-5D.

Setting: A psychiatric outpatient clinic in Stockholm, Sweden.

Participants: Participants were 126 individuals with social anxiety disorder.

Primary outcome measures: Changes in EQ-5D and costs.

Interventions: Participants received either CBGT or ICBT for a duration of 15 weeks.

Results: Results: ICBT minimized healthcare costs and demonstrated health improvements within the non-inferiority margin. Assuming a practical work capacity for personnel varying between 100%, 80% and 50% of theoretical full capacity, the cost for ICBT varied in the

1
2
3 range between 400 €, 463 € and 654 €, while the cost for CBGT varied between 699 €, 806 €
4
5 and 1134 €. Within-group effect size was -0.36 (95% CI: -0.70 to -0.01) for ICBT and -0.25
6
7 (95% CI: -0.60 to 0.10) for CBGT. Mean use of effective psychologist time in ICBT was
8
9 189.60 (SD = 53.77) minutes compared to 499.78 (SD = 30.91) in the CBGT group.
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14 **Conclusions:** In treatment of SAD, ICBT is equally effective but is associated with more
15
16 efficient staff utilization and less costs compared with CBGT. From a health care provider
17
18 perspective, ICBT is an advantageous treatment option.
19

20 21 22 23 **Strengths and limitations of this study**

- 24 • Randomized controlled design.
- 25 • Low attrition rates.
- 26 • Includes long-term follow-up data.
- 27 • It may be difficult to generalize time and cost estimates of resource use to other
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60 settings.

40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 <Introduction>

Common mental health problems including depression and anxiety disorders are a major concern globally, and in the UK affecting approximately 17% of the population (1). The cost of these problems in England alone has been estimated at £105.2 billion (approximately 121 billion Euros) which includes costs associated with reduced health-related quality of life, lost productivity and social and health care costs (2). Social anxiety disorder (SAD) is one of the most prevalent anxiety disorders with a 12-month prevalence of 2.8%-7.1% and a lifetime prevalence of 5%-12.1% (3-5). SAD is associated with functional impairment and typically

1
2
3 follows a chronic course if untreated (6-9). The National Institute for Health and Care
4
5 Excellence (NICE) in the UK recommends cognitive behavioural therapy (CBT) as the first-
6
7 line treatment option for SAD (10). Cognitive behavioural group therapy (CBGT) is an
8
9 effective format of CBT provision in the treatment of SAD (11, 12). Although many patients
10
11 prefer psychological therapies to medication, access is limited in both primary and secondary
12
13 care (13).

14
15
16 Recently, Internet-based cognitive behaviour therapy (ICBT) has emerged as an
17
18 empirically supported treatment for SAD with effect sizes on par with those of CBGT and
19
20 tested in at least 16 randomized controlled trials (14). Our research group has previously
21
22 compared ICBT to CBGT in a non-inferiority trial and found ICBT to be at least as effective
23
24 as CBGT (15). At post-treatment, it was observed that 55% (95% CI, 42.5%–66.9%) of
25
26 patients having received ICBT were classified as responders, compared to 34% (95% CI,
27
28 22.1%–45.7%) having received CBGT. At six-month follow-up, the corresponding numbers
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30 were 64% (95% CI, 52.3%–75.8%) in the ICBT group and 45% (95% CI, 32.8%–57.6%) in
31
32 the CBGT group.
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34

35
36 Even though some previous studies indicate that ICBT for SAD can be cost-
37
38 effective (16, 17), evidence is lacking concerning health economic evaluations from a health
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40 care provider perspective. In the present study, we used the time-driven activity based costing
41
42 method, which takes into account all costs related to the treatment from the health care
43
44 provider's perspective. To our knowledge, this has not been previously done when evaluating
45
46 ICBT for SAD.
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48

49
50 In health economic evaluations, a choice is often made between four types of
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52 methods: a cost-benefit analysis (CBA) in which both benefits and costs are expressed in
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54 monetary terms; a cost-effectiveness analysis (CEA) where costs and treatment effects are
55
56 compared; a cost-utility analysis which is similar to CBA and CEA but where benefits is
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2
3 expressed in terms of quality-adjusted life years (QALYs); and finally, cost-minimisation
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5 analysis (CMA), which focuses on comparing the costs of different treatments with
6
7 previously demonstrated equivalence in clinical efficacy.
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9
10 Given the equivalence of both treatment formats in terms of health
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12 improvements previously demonstrated in a randomized controlled trial (15), the purpose of
13
14 this study was to assess whether ICBT may help minimize the costs of healthcare use relative
15
16 to CBGT. This was done by using both data from a randomized controlled trial and
17
18 additionally collected data on resource use. In contrast to previous health economic
19
20 evaluations (16, 18), the present study adopted a health care provider perspective using time-
21
22 driven activity based costing (TDABC) methodology. If ICBT is found to help minimize the
23
24 costs of healthcare use relative to CBGT, such internet-based interventions have the potential
25
26 to increase access to psychological therapy in psychiatry and primary care and could represent
27
28 an efficient alternative psychological treatment for SAD.
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30

31 32 33 34 <Method>

35 36 <Design>

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38 This was a cost-minimisation analysis adopting a healthcare provider perspective, conducted
39
40 alongside a non-inferiority trial within the context of a parallel group study with unrestricted
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42 randomization in 1:1 ratio (ICBT or CBGT). Costs measured from a healthcare provider
43
44 perspective were estimated using time-driven activity based costing alongside with health
45
46 status over four years from baseline measured with EQ-5D. All costs were estimated based on
47
48 thorough assessment of the costs associated with ICBT when delivered in regular care (which
49
50 was implemented at the clinic after the RCT); this was done in order not to underestimate the
51
52 treatment costs. The trial was registered at clinicaltrials.gov (identifier NCT00564967). The
53
54 main outcome study has been reported elsewhere (15).
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5 <Recruitment, inclusion criteria and participants>
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7 The study was conducted at a public ICBT unit in Stockholm, Sweden (Stockholm Health
8 Care Services). Participants were recruited by self-referral (n = 97) or by referral from
9 primary care physicians and psychiatrists (n = 29). The study protocol was approved by the
10 Regional Ethical Review Board in Stockholm and informed consent was obtained from all
11 participants. The recruitment took place between 2007 and 2009. The participant flow
12 throughout the trial is presented in the main outcome study (15).
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23 <Treatments>
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25 ≤ Internet-based cognitive behaviour therapy (ICBT)>
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27 The internet-delivered treatment was based on and adapted from a treatment originally
28 developed by Andersson and colleagues and followed a CBT model developed for individual
29 therapy of SAD (19-21). The treatment content was accessed as text modules similar to
30 chapters in self-help bibliotherapy. Each chapter corresponded to a CBT session with a
31 specific theme such as cognitive restructuring, graded exposure or behavioral experiments,
32 coupled with homework assignments. Patients received supportive email feedback from a
33 psychologist after each module. The duration of the internet-based intervention was 15 weeks,
34 and therapists were instructed to restrict time spent on each patient to approximately 10
35 minutes per week.
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49 ≤ Cognitive behavioural group therapy (CBGT)>
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51 The group CBT for SAD followed the protocol developed by Heimberg and Becker (2002).
52 The treatment was equally long as the ICBT (i.e. 15 weeks) consisting of one initial
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3 individual session followed by 14 group sessions. Each session was 2.5 hours long and led by
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5 therapists trained in CBT. Each group consisted of six to seven patients.
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7

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9
10 <Outcome measure>

11 EuroQol (EQ-5D) index values were used to assess improvements in health-related quality of
12
13 life (EuroQol-Group, 1990). The EQ-5D is non-disease specific and measures five health
14
15 domains of importance to quality of life: mobility, self-care, usual activities, pain/discomfort
16
17 and anxiety/depression.
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21
22 <Resource use>

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24 Resource use was estimated by using a bottom-up approach where the clinical and
25
26 administrative activities performed throughout the treatment delivery cycle were first
27
28 documented through process maps. This allowed us to identify resource use in terms of type
29
30 (e.g. personnel, hospital space, IT) and time (measured in minutes and collected through time
31
32 studies and interviews). The time studies and estimations on resource use were conducted at
33
34 the treatment facility after the original RCT had been completed, i.e. when the treatment had
35
36 been implemented as routine care.
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41
42 <Costs>

43
44 TDABC was used to determine the costs associated with ICBT and CBGT from a healthcare
45
46 provider perspective (22). Based on estimated resource use (described above), the capacity
47
48 cost rate (i.e. cost per minute) was calculated for each resource. The overall approach for
49
50 calculating capacity cost rates for each resource involved the allocating of costs such as
51
52 hospital space, supervision, IT (computers, email, services, etc.) and management evenly per
53
54 minute. Costs for hospital space were calculated as the square meter price divided by floor
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3 space per staff category and joint surfaces were then allocated. Shared costs included
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5 management as well as shared unit administration. Finally, hospital costs for security and
6
7 safety were also included. The minute cost for each personnel category therefore include these
8
9 costs. I.e., the minute cost for a psychologist include the allocated costs for IT usage
10
11 (including hardware and software), hospital space usage, etc. Economic data for these costs
12
13 was provided from the general ledger for the psychiatric department. However, costs related
14
15 to prior training of staff and the actual software development of the ICBT platform was not
16
17 included; rather the day-to-day costs of administering treatment was the focus of this study.
18
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21 The minute-cost for a psychologist was calculated by dividing the total annual
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23 salary by the total number of minutes worked. Since not all time worked was available for
24
25 clinical care due to meetings, training and breaks etc., the practical capacity of each staff
26
27 category was estimated to be 80% of the actual number of worked hours, which is typically
28
29 used as a standard assumption (22). A sensitivity analysis have been performed to study the
30
31 effects of changing this rate down to 50% or up to 100%, presented in a cost-effectiveness
32
33 acceptability curve to summarise the uncertainty of the estimates in the cost-effectiveness
34
35 analysis.
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39 Finally, the total cost of each treatment episode was calculated for each patient
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41 by multiplying the minute cost for each resource with the total number of minutes spent on
42
43 each activity and then summing across all resources. Time estimates (and thus costs) not
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45 related to psychologists (e.g. assessments by medical doctors and administrative tasks by
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47 nurses and secretaries outside of treatment) were assumed to be similar in both groups. In
48
49 addition to calculating actual costs, costs were also estimated when discounted at annual rates
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51 of 3% and 5% respectively, and presented in €, year 2017 values.
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56 <Cost-minimisation analysis>
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3 Since the main outcome study have demonstrated equivalence in treatment efficacy, we chose
4 to conduct a CMA where costs per course of treatment from a healthcare provider perspective
5 were calculated and compared between treatment groups; if total costs were reduced by more
6 efficient resource use, cost-minimisation may be achieved (23). In order to avoid biased
7 estimation of uncertainty, we have used the statistical methods of cost-effectiveness to
8 evaluate the joint distributions of costs and benefits.
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16 The cost-effectiveness analysis was conducted through the following steps: (1)
17 calculation of costs and effects of each intervention (2) calculation of the differences in cost
18 and differences in effects and (3) calculating the incremental cost and incremental benefit of
19 ICBT versus CBGT and (4) and presenting the distribution of cost/effect differences on a
20 cost-effectiveness plane with confidence interval estimation around the calculated ratio (24).
21 If ICBT is found to be equally effective but less costly, it will be located in the south
22 quadrants of the cost-effectiveness plan close to the y-axis. The question then arises whether
23 the cost saving of ICBT is worth the health loss or health gain.
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40 <Sensitivity analysis>

41 A probability sensitivity analysis was performed to estimate the uncertainty surrounding the
42 cost-effectiveness ratios. Confidence ellipses at 50%, 75%, and 95% were calculated and
43 cost-effectiveness acceptability curves (CEACs) were constructed to represent the uncertainty
44 around the estimate (25) in accordance with recommended guidelines (26). Incremental net
45 benefit (INB) was used to interpret the CEAC, where the slope of the net monetary benefits
46 (NMB) curve represents the difference in effects between ICBT and CBGT.
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56 <Results>

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3 <Outcomes>
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5 As previously reported (18) the between-group effect size on EQ5D was -0.18 (95% CI: -0.53
6 to 0.17), indicating equivalence in treatment effects. The within-group effect size was -0.36
7 (95% CI: -0.70 to -0.01) for ICBT and -0.25 (95% CI: -0.60 to 0.10) for CBGT. Treatment
8 adherence was similar across treatment conditions; out of possible 15 sessions and modules
9 respectively, mean number of attended sessions was 9.40 (SD = 4.87) in the CBGT group
10 and 9.33 (SD = 4.95) in the ICBT group. As previously reported, number of attended
11 treatment sessions/completed modules was positively related to treatment outcome (27).
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23 <Resource use>
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25 An independent-samples t-test was conducted to compare psychologist time in ICBT and
26 CBGT treatments. There was a significantly lower use of psychologist time in ICBT (M =
27 189.60, SD = 53.77) compared to CBGT (M = 499.78, SD = 30.91), with a mean difference
28 of 310.16 (95% CI: 248.47 to 371.86) minutes; $t(124) = 9.95, p < .001$. Table 1 presents
29 average number of minutes consumed per resource category over a complete cycle of care.
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43 INSERT TABLE 1 ABOUT HERE.
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45 <Costs and cost-minimisation>
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47 Assuming a practical capacity of 80% of full theoretical capacity for healthcare staff, mean
48 total healthcare costs are reported in Table 1. Taking into account the complete treatment
49 episode, total estimated cost for ICBT was 463 € (95% CI: 446 € to 480 €) per patient
50 compared with 806 € (95% CI: 730 € to 883 €) for CBGT. Table 1 also presents the average
51 costs for each resource involved in the complete care episode, where costs of hospital space,
52 supervision, IT and management has been allocated over each staff category.
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3 Estimated capacity cost rates (cost per minute) for each staff category are
4 presented in Table 2 for different assumptions of practical capacity. Estimations indicate that
5 the cost per minute increases as less time is spent on clinical work.
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12 INSERT TABLE 2 ABOUT HERE.
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16 Estimated healthcare cost for different assumptions of practical capacity is
17 presented in Table 3. Assuming that staff spends 100% of their theoretical full capacity on
18 clinical work directly related to the treatment processes, the total cost of CBGT is estimated at
19 699 € (95% CI: 632 € to 765 €) compared to 400 € (95% CI: 386 € to 415 €) for ICBT.
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28 INSERT TABLE 3 ABOUT HERE.
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32 The estimated cost-savings of ICBT relative to CBGT at different assumptions
33 of practical capacity is presented in Table 4, ranging from 299 € (95% CI: 232 € to 356 €) to
34 481 € (95% CI: 374 € to 587 €). Assuming a practical capacity of 80%, the cost-saving is
35 estimated to be 343 € (95% CI: 267 € to 420 €).
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44 INSERT TABLE 4 ABOUT HERE.
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47 Fig. 1 illustrates confidence-ellipses around the point estimate; as the 95% and
48 75% confidence ellipses occupy both the south-east (SE) and south-west (SW) quadrants, this
49 indicates that the ICBT treatment was equally effective but less costly relative to the CBGT
50 intervention; the entire density within the ellipses involves cost-savings. Table 5 presents
51 costs and mean differences when taking account of time (at an assumption of 80% practical
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3 capacity), assuming 3% and 5% annual discount rates; when costs were discounted at 3%, the
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5 mean difference was 305 € (95% CI: 237 € to 373 €) and 283 € (95% CI: 220 € to 345 €) at a
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7 5% discount rate.
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12 INSERT TABLE 5 ABOUT HERE
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16 INSERT FIG. 1 ABOUT HERE
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21 Cost-effectiveness acceptability curves (CEAC) are presented in **Fig. 2**, including a
22
23 sensitivity analysis of different assumptions of practical capacity applied in the calculation of
24
25 cost rates. The CEACs indicate the probability that ICBT is cost-effective compared with
26
27 CBGT for a given value of the maximum willingness to pay (WTP) for a gained unit of
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29 health-related quality of life. As can be seen, the probability for ICBT being cost-effective is
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31 high regardless of WTP.
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36 INSERT FIG. 2 ABOUT HERE
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41 A graphical representation of the net benefit is illustrated in Fig. 3. The uncertainty of the
42
43 value of the intervention gets larger as the WTP for the clinical outcome increases; this is
44
45 reflected in the increasing CI of the INB. The positive NMBs suggest that the intervention is
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47 cost-effective at four year follow-up assessment.
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52 INSERT FIG. 3 ABOUT HERE
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56 <Discussion>
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3 < *Principal findings* >
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5 The objective of this study was to assess whether ICBT is less costly relative to CBGT in the
6
7 treatment of patients with SAD. While clinical treatment effects were equivalent, healthcare
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9 costs were lower in the ICBT group (463 €) compared with the CBGT group (806 €),
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11 assuming a practical capacity of around 80%. This study thus showed that ICBT for SAD is
12
13 clearly less costly compared to CBGT from a health care provider perspective. These results
14
15 add to the previous body of research demonstrating that ICBT is associated with improved
16
17 economic outcomes. (28) However, most health economic evaluations have mainly been
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19 performed from a societal perspective. By using a healthcare provider perspective, and a
20
21 TDABC costing approach, this study may help to develop a greater understanding of the costs
22
23 incurred by the resources used throughout the clinical care of patients and by their
24
25 administrative processes.
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32 < *Implications for policy and practice* >
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34 Evidence suggests that ICBT is equally effective as the more commonly provided face-to-face
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36 CBT, not only for SAD (15, 29) but for a wide range of mood and anxiety disorders (30),
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38 while requiring less healthcare resources. Therefore, ICBT may have a number of advantages
39
40 that would benefit both health care providers and patients. First, since ICBT requires
41
42 significantly less therapist time, each therapist is able to treat more patients simultaneously,
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44 consequentially increasing treatment availability and shortening waiting lists. Another
45
46 advantage is that ICBT overcomes geographic barriers for patients and thus to provide access
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48 to evidence based psychological treatment at more equal opportunities. Finally, accessing
49
50 therapy sessions online is practical and more economical for patients because it enables them
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52 to work with the treatment at their own convenience, and not having to take time off work for
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54 making visits to their healthcare provider. To further increase access to evidence based
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3 psychological interventions for SAD, ICBT may be considered as an alternative to face-to-
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5 face psychological therapies as an initial step within a stepped care approach. This should also
6
7 be considered for other evidence based ICBT applications such as in depression and panic
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9 disorder.
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14 <Strengths and limitations>

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16 The main strengths of the present study were the randomized controlled design, the direct
17
18 comparison of ICBT against face-to-face CBT, and the low attrition rates. However, the study
19
20 had some limitations.
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23 First, the use of TDABC as a costing methodology in healthcare is relatively
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25 new, particularly within mental health care; it has been more commonly used in industry. (31-
26
27 33) Therefore, its validity may be difficult to evaluate at this stage. Also, although CBT
28
29 treatment delivery may be similar across different healthcare providers, supporting
30
31 administrative processes and clinical practices might differ significantly. As a result, it may
32
33 be difficult to generalize time and cost estimates of the total healthcare episode to other
34
35 settings and healthcare providers.
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39 A second limitation relates to difficulties in arriving at accurate time estimates
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41 of resource use and activities performed. Since actual logging of time requires an electronic
42
43 measurement system, only accurate timing of the amount of time each psychologist spent with
44
45 each patient in ICBT could be recorded (thus providing measures of variability), whereas
46
47 other clinical and administrative processes were based on estimated average standard times.
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50 Third, parts of the time studies and estimations on resource use were carried out
51
52 several years after the original RCT, i.e. when the treatment had been implemented as routine
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54 care. Although administrative routines and processes have remained more or less similar over
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56 the years, there may still be minor differences when compared to how the administrative
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3 processes were during the RCT. Therefore, difficulties in retrieving exact cost data may add
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5 to the uncertainty around cost estimates.
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8 Fourth, since our study is based on a non-inferiority trial with observed
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10 equivalence in treatment effects, the confidence interval suggested some uncertainty around
11
12 the estimated effect. This concern in cost-effectiveness analyses have been discussed by
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14 Briggs and O'Brien (34); in line with the recommendations outlined in the article, we have
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16 aimed at providing an appropriate representation of uncertainty using confidence-ellipses on
17
18 the cost-effectiveness plane.
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21 Finally, we will comment on the choice of cost-minimisation analysis in the
22
23 present study. Economic evaluations in healthcare compare treatment options or technologies
24
25 in terms of clinical effects and costs, typically resulting in a cost-effectiveness ratio. The
26
27 incremental cost-effectiveness ratio (ICER) summarises the cost-effectiveness of a treatment
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29 relative to an alternative by calculating the difference in costs between the two divided by the
30
31 difference in effects (23). We have previously estimated an ICER from a societal perspective
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33 using the formula $(C_{ICBT} - C_{CBGT}) / (E_{ICBT} - E_{CBGT})$, where C_{ICBT} and E_{ICBT} represents the cost
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35 and effect in the ICBT group and where C_{CBGT} and E_{CBGT} represent the cost and effect in the
36
37 CBGT group (16, 18). The difference between cost-effectiveness analysis (CEA) and cost-
38
39 minimisation analysis (CMA) has been further discussed elsewhere (35); a full cost-
40
41 effectiveness analysis is often a preferred method to assess differences in both costs and
42
43 effects. However, in the context of a non-inferiority trial where treatments have been found to
44
45 be equally effective, CMA may be an appropriate method to analyze cost differences (23),
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47 since the focus of interest is which treatment is less expensive. Since both treatments in this
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49 study were found to have equivalent efficacy, estimating an ICER may not be the optimal
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51 approach as the ICER approaches infinity when effect difference is close to zero. However, if
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3 ICBT can reduce resource use in treatment of SAD, it may lower healthcare costs. Therefore,
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5 a cost-minimisation approach was considered more appropriate in this case.
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8
9 <Conclusion>
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11 In treatment of SAD, ICBT is equally effective but is associated with more efficient staff
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13 utilization and considerably lower costs compared with CBGT. From a health care provider
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15 perspective, ICBT is an advantageous treatment option.
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8
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15
16 interpreted the data and drafted the paper. EH designed the study, developed the SAD
17
18 treatment, performed the analyses, and drafted the paper. NL and BL designed the study,
19
20 interpreted the data, and drafted the paper.
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54 **Competing interests:** None declared.
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3 **Data sharing statement:** Study data are stored at the repository of Karolinska Institutet. With
4 respect to the legal framework regulating access to research data in Sweden, the data are not
5 freely accessible due to regulations regarding personal integrity in research, public access and
6 privacy; each request is therefore assessed by the Karolinska Institutet ethics committee, and
7 approval of data access can be given after this assessment. To request data, contact Karolinska
8 Institutet by e-mail at info@ki.se, or at Karolinska Institutet, SE-171 77, Stockholm, Sweden.
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24 **Fig. 1.** *Mean differences in costs and gained health-related quality of life.*
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28 Note. Each confidence-ellipse represents regions with a 50%, 75% or 95% certainty around
29 the mean difference in cost and effect. Abbreviations: ICBT, internet-based cognitive
30 behaviour therapy.
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37 **Fig. 2.** *Cost-effectiveness acceptability curves for different assumptions of practical capacity.*
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40 Note. The cost-effectiveness acceptability curves shows for different assumptions of
41 personnel's practical work capacity of their full theoretical capacity, the probabilities that
42 ICBT is cost-effective with changes in the amount that society is willing to pay for a unit
43 increase in health related quality of life, considering healthcare costs.
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51 **Fig. 3.** *Net monetary benefit curves and 95% confidence intervals at 4-year follow-up.*
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Tables

Table 1. Estimation of a patient's cost over a complete cycle of care for treating social anxiety disorder with ICBT or with CBGT

| | Coordinating nurse | | Psychiatrist | | Resident physician | | Psychologist | | Medical secretary | | Total | |
|--|--------------------|--------------|-----------------|--------------|--------------------|--------------|-----------------|--------------|-------------------|--------------|-----------------|--------------|
| | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost | Average minutes | Average cost |
| ICBT | | | | | | | | | | | | |
| Registration and verification | 11 | 13€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 11 | 13€ |
| Diagnostic assessment | 0 | 0€ | 20 | 43€ | 80 | 112€ | 0 | 0€ | 0 | 0€ | 100 | 154€ |
| Supervision meeting / discussion | 0 | 0€ | 3 | 6€ | 3 | 4€ | 1 | 1€ | 0 | 0€ | 7 | 11€ |
| Supplementary psychological assessment | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 7€ | 0 | 0€ | 5 | 7€ |
| Administrating treatment activation | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 41 | 41€ | 41 | 41€ |
| ICBT intervention (online) | 0 | 0€ | 0 | 0€ | 0 | 0€ | 82 | 102€ | 0 | 0€ | 82 | 102€ |
| ICBT intervention (offline) | 0 | 0€ | 0 | 0€ | 0 | 0€ | 77 | 95€ | 0 | 0€ | 77 | 95€ |
| Administrative preparation for follow-up visit | 3 | 3€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 3 | 3€ |
| Post-treatment clinical visit | 0 | 0€ | 0 | 0€ | 0 | 0€ | 24 | 30€ | 0 | 0€ | 24 | 30€ |
| Discharge | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 5€ | 5 | 5€ |
| Total | 14 | 17€ | 23 | 49€ | 83 | 116€ | 190 | 235€ | 46 | 46€ | 355 | 463€ |
| CBGT | | | | | | | | | | | | |
| Registration and verification | 11 | 13€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 11 | 13€ |
| Diagnostic assessment | 0 | 0€ | 20 | 43€ | 80 | 112€ | 0 | 0€ | 0 | 0€ | 100 | 154€ |
| Supervision meeting / discussion | 0 | 0€ | 3 | 6€ | 3 | 4€ | 1 | 1€ | 0 | 0€ | 7 | 11€ |
| Supplementary psychological assessment | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 7€ | 0 | 0€ | 5 | 7€ |

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| 5 | CBGT intervention | 0 | 0€ | 0 | 0€ | 0 | 0€ | 470 | 582€ | 0 | 0€ | 470 | 582€ |
| 6 | Administrative preparation for follow-up visit | 3 | 3€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 3 | 3€ |
| 7 | Post-treatment clinical visit | 0 | 0€ | 0 | 0€ | 0 | 0€ | 24 | 30€ | 0 | 0€ | 24 | 30€ |
| 8 | Discharge | 0 | 0€ | 0 | 0€ | 0 | 0€ | 0 | 0€ | 5 | 5€ | 5 | 5€ |
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| 11 | Total | 14 | 17€ | 23 | 49€ | 83 | 116€ | 500 | 619€ | 5 | 5€ | 625 | 806€ |
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HEALTH ECONOMIC EVALUATION OF ICBT FOR SAD

Table 2. Cost rates (€/minute) at different assumptions of practical capacity.

| Practical capacity assumption | Medical secretaries | Psychiatrist | Resident Physician | Psychologists | Coordinating nurse |
|-------------------------------|---------------------|--------------|--------------------|---------------|--------------------|
| 100% | 0,90 | 1,79 | 1,19 | 1,08 | 1,06 |
| 80% | 1,02 | 2,13 | 1,40 | 1,24 | 1,21 |
| 50% | 1,38 | 3,14 | 2,02 | 1,73 | 1,67 |

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HEALTH ECONOMIC EVALUATION OF ICBT FOR SAD

Table 3. Estimated healthcare cost for different assumptions of practical capacity.

| | Assumed practical capacity | N | Cost (€) | 95% Confidence Interval | |
|------|----------------------------|----|----------|-------------------------|-------|
| | | | | Lower | Upper |
| CBGT | 50% | 62 | 1134 | 1027 | 1241 |
| | 80% | 62 | 806 | 730 | 883 |
| | 100% | 62 | 699 | 632 | 765 |
| ICBT | 50% | 64 | 654 | 630 | 677 |
| | 80% | 64 | 463 | 446 | 480 |
| | 100% | 64 | 400 | 386 | 415 |

HEALTH ECONOMIC EVALUATION OF ICBT FOR SAD

Table 4. Estimated mean differences in healthcare cost between ICBT and CBGT for different assumptions of practical capacity

| Assumed practical capacity of full theoretical capacity | Mean cost difference (€) | 95% Confidence Interval of the Difference | |
|---|--------------------------|---|-------|
| | | Lower | Upper |
| 50% | 481 | 374 | 587 |
| 80% | 343 | 267 | 420 |
| 100% | 299 | 232 | 365 |

Note. Independent-samples t-test were conducted to compare total costs for ICBT and CBGT for different levels of assumed practical capacity in relation to theoretical full capacity, indicating significant differences in healthcare costs; $t(124)=8.9$, $p < .001$.

HEALTH ECONOMIC EVALUATION OF ICBT FOR SAD

Table 5. *Estimation of actual and discounted costs of care for treating social anxiety disorder with ICBT or with CBGT*

| | Group | N | Mean cost, € | SD | Mean difference, € | 95% Confidence Interval of the Difference | |
|--|-------|----|--------------|-----|--------------------|---|-------|
| | | | | | | Lower | Upper |
| Total costs, actual | CBGT | 62 | 806 | 302 | | | |
| | ICBT | 64 | 463 | 67 | 343 | 267 | 420 |
| Total costs, discounted at 3% per year | CBGT | 62 | 717 | 268 | | | |
| | ICBT | 64 | 411 | 59 | 305 | 237 | 373 |
| Total costs, discounted at 5% per year | CBGT | 62 | 663 | 248 | | | |
| | ICBT | 64 | 381 | 55 | 283 | 220 | 345 |

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HEALTH ECONOMIC EVALUATION OF ICBT FOR SAD

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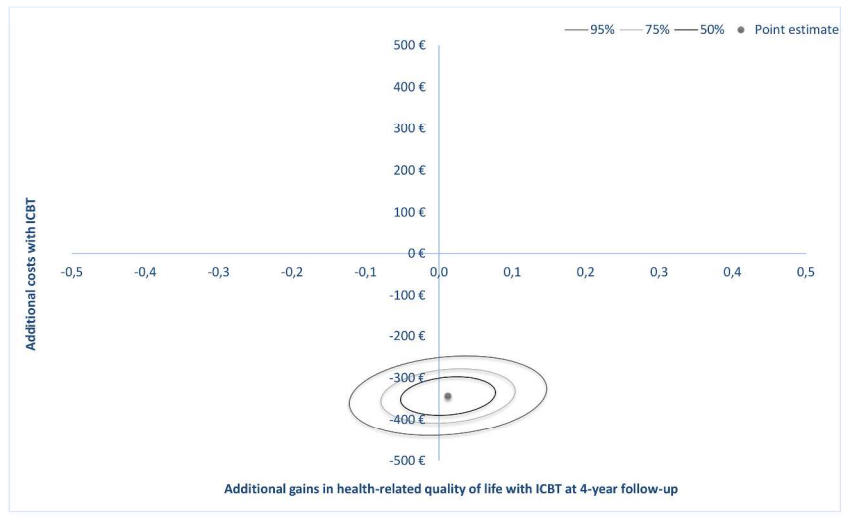


Fig. 1. Mean differences in costs and gained health-related quality of life.

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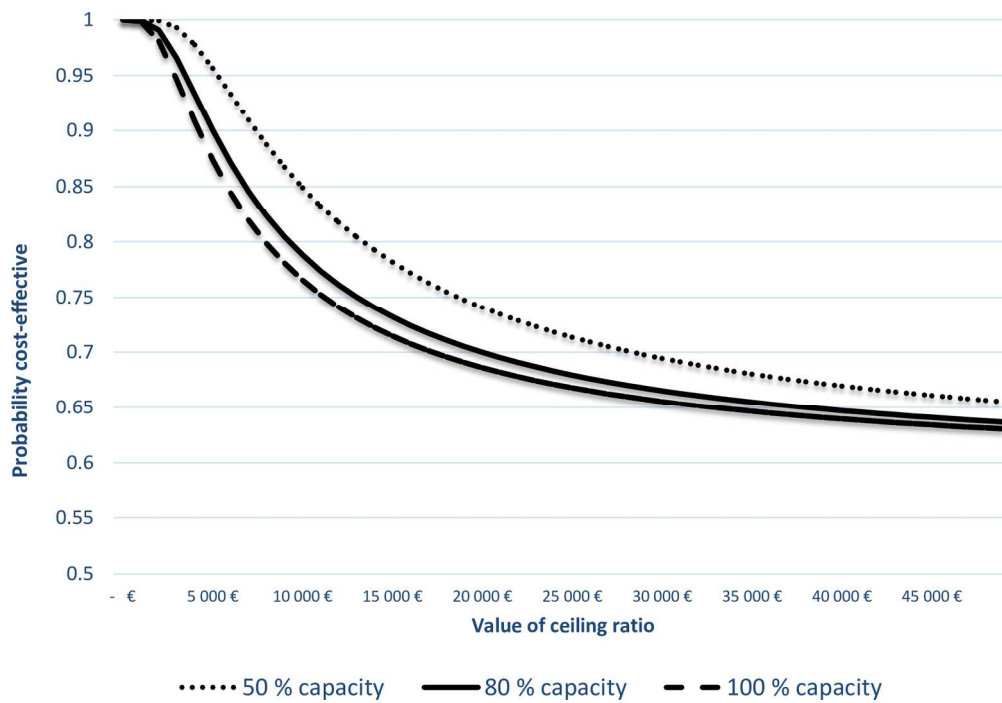


Fig. 2. Cost-effectiveness acceptability curves for different assumptions of practical capacity.

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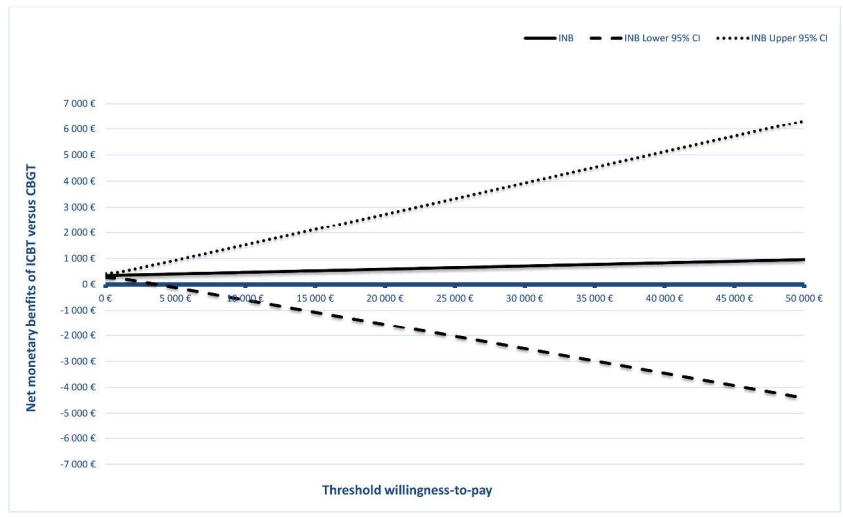


Fig. 3. Net monetary benefit curves and 95% confidence intervals at 4-year follow-up

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Review only

CHEERS checklist—Items to include when reporting economic evaluations of health interventions

| Section/item | Item No | Recommendation | Reported on page No/ line No |
|--|---------|--|-----------------------------------|
| Title and abstract | | | |
| Title | 1 | Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared. | page 1, line 2 |
| Abstract | 2 | Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions. | page 2, line 1 to 24 |
| Introduction | | | |
| Background and objectives | 3 | Provide an explicit statement of the broader context for the study. | page 3, line 7 to page 4, line 18 |
| | | Present the study question and its relevance for health policy or practice decisions. | page 4, line 9 to 18 |
| Methods | | | |
| Target population and subgroups | 4 | Describe characteristics of the base case population and subgroups analysed, including why they were chosen. | page 4, line 20 and continued. |
| Setting and location | 5 | State relevant aspects of the system(s) in which the decision(s) need(s) to be made. | page 4, line 20 and continued. |
| Study perspective | 6 | Describe the perspective of the study and relate this to the costs being evaluated. | page 6, line 21 and continued. |
| Comparators | 7 | Describe the interventions or strategies being compared and state why they were chosen. | page 4, line 20 and continued |
| Time horizon | 8 | State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate. | page 5, line 1 |
| Discount rate | 9 | Report the choice of discount rate(s) used for costs and outcomes and say why appropriate. | page 7, line 11 |
| Choice of health outcomes | 10 | Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed. | page 6, line 9 |
| Measurement of effectiveness | 11a | <i>Single study-based estimates</i> : Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data. | page 7, line 24 |
| | 11b | <i>Synthesis-based estimates</i> : Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data. | |
| Measurement and valuation of preference based outcomes | 12 | If applicable, describe the population and methods used to elicit preferences for outcomes. | not applicable |
| Estimating resources and costs | 13a | <i>Single study-based economic evaluation</i> : Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | |

| Section/item | Item No | Recommendation | Reported on page No/ line No |
|--|---------|---|---------------------------------------|
| | 13b | <i>Model-based economic evaluation:</i> Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | not applicable |
| Currency, price date, and conversion | 14 | Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate. | page 7, line 12 |
| Choice of model | 15 | Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended. | page 7, line 14 |
| Assumptions | 16 | Describe all structural or other assumptions underpinning the decision-analytical model. | |
| Analytical methods | 17 | Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty. | page 7, line 19 |
| Results | | | |
| Study parameters | 18 | Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended. | page 8, lines 11 to 24 |
| Incremental costs and outcomes | 19 | For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios. | figure 1; page 8, lines 11 to 24 |
| Characterising uncertainty | 20a | <i>Single study-based economic evaluation:</i> Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective). | figure 1 |
| | 20b | <i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions. | not applicable |
| Characterising heterogeneity | 21 | If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information. | not applicable |
| Discussion | | | |
| Study findings, limitations, generalisability, and current knowledge | 22 | Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge. | page 9, line 3 to page 11, line 21 |

| Section/item | Item No | Recommendation | Reported on page No/ line No |
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| Other | | | |
| Source of funding | 23 | Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support. | page 12, line 16 |
| Conflicts of interest | 24 | Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations. | Information provided via the submission system |

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist