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Published in:
Psychiatry Research

DOI:
[10.1016/j.psychres.2023.115692](https://doi.org/10.1016/j.psychres.2023.115692)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2024

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Vollbehr, N. K., Stant, A. D., Hoenders, H. J. R., Bartels-Velthuis, A. A., Nauta, M. H., Castelein, S., Schroevers, M. J., de Jong, P. J., & Ostafin, B. D. (2024). Cost-effectiveness of a mindful yoga intervention added to treatment as usual for young women with major depressive disorder versus treatment as usual only: Cost-effectiveness of yoga for young women with depression. *Psychiatry Research*, 333, Article 115692. <https://doi.org/10.1016/j.psychres.2023.115692>

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Cost-effectiveness of a mindful yoga intervention added to treatment as usual for young women with major depressive disorder versus treatment as usual only

Cost-effectiveness of yoga for young women with depression

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ARTICLE INFO

Trial registration: Clinical Trials, NCT03388177, <http://www.clinicaltrials.gov/>.

Keywords:

Cost effectiveness

Depression

Women

Yoga

Randomized controlled trial

ABSTRACT

In a randomized controlled trial in the Netherlands, we studied the (cost)effectiveness of adding a mindful yoga intervention (MYI+TAU) to treatment as usual (TAU) for young women with major depressive disorder (MDD). In this paper, we present the results of the economic analyses. Societal costs and health outcomes were prospectively assessed during 15 months for all randomized participants ($n = 171$). Symptoms of depression (Depression Anxiety and Stress Scales; DASS) and quality adjusted life years (QALYs) were used as health outcomes in the economic analyses. Mean total societal costs during the 15 months of the study were €11.966 for the MYI+TAU group and €13.818 for the TAU group, differences in mean total societal costs were not statistically significant. Health outcomes (DASS and QALY) were slightly in favour of MYI+TAU, but differences between groups were not statistically significant. Combining costs and health outcomes in cost-effectiveness analyses indicated that MYI+TAU is likely to be cost-effective compared to TAU which was confirmed by sensitivity analyses. Although there were limitations in the cost-effectiveness analysis, findings from this study suggest that MYI+TAU warrants future attention for the potential to be cost-effective compared to TAU for young women with MDD.

1. Introduction

Depression is the third leading cause of disease burden worldwide (James et al., 2018). The 12-month prevalence of depression in women is higher than that of men (Ferrari et al., 2013). Especially young women (aged 18–34) are at relatively high risk of developing major depressive disorder (MDD) (De Graaf et al., 2012). In addition to individual suffering, there are also considerable financial consequences for society due to MDD (Koenig et al., 2020). This is mainly because of higher healthcare utilization and spending and because of increased

absenteeism from and reduced productivity at work (Donohue and Pincus, 2007). Improved treatment for depression could lead to lower economic costs (Kessler, 2012). Offering a combination of interventions might enhance treatment outcomes, as is the case for patients with severe depression, for whom the combination of medication and psychotherapy is recommended in the Netherlands (Spijker et al., 2013). Economic analyses of this guideline-recommended treatment for moderate to severe depression showed that it most likely is cost-effective (Federation of Medical Specialists [Federatie Medisch Specialisten], 2013). Costs for each gained QALY for guideline-recommended

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<https://doi.org/10.1016/j.psychres.2023.115692>

Received 25 April 2023; Received in revised form 22 December 2023; Accepted 24 December 2023

Available online 30 December 2023

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treatment compared to usual care are €7000, which is relatively low, though higher than for mild depression where for the majority of patients a single intervention is offered (Federation of Medical Specialists [Federatie Medisch Specialisten], 2013). This offers some support for the idea that adding an intervention to depression treatment in the Netherlands might be cost-effective.

One intervention that especially represents a promising intervention for young women with depression is mindful yoga (Falsafi, 2016; Woolery et al., 2004). Mindful yoga consists of a combination of physical postures, breathing, and meditation practices, including the cultivation of a mindful (non-judgmental) awareness of body sensations and thoughts (Anderson and Sovik, 2000).

Surveys among yoga practitioners in the United States and the United Kingdom have found that yoga is popular among young women (Nalbant et al., 2022). This suggests that yoga could be an attractive form of adjunctive treatment for young women with depression. In addition, mindful yoga might target mechanisms that seem to be involved in the onset and maintenance of depression, thereby reducing symptoms of depression. These mechanisms include rumination (Nolen-Hoeksema, 2000) and self-criticism (Sherry et al., 2014), both of which have been found to be more present in women than in men (Powers et al., 2004), which might partially explain the observed sex differences in depression (Hamilton et al., 2015). Initial research supports this idea, as yoga participants report lower rumination (Kinser et al., 2014; Schuver and Lewis, 2016) and more self-compassion (the opposite of self-criticism; Carmody and Baer, 2008). In sum, as young women are particularly at risk for developing MDD, mindful yoga might be a potential attractive and beneficial adjunctive form of treatment, targeting mechanisms that are associated with depression and more present in (young) women.

Cost-effectiveness analyses are important for making policy decisions about allocating treatment for depression, based on information about incremental costs and health benefits of these treatments (Barrett et al., 2005). Among standard treatments for depression, cost-effectiveness analyses have been conducted and shown benefits for anti-depressant medication (Khoo et al., 2015; Ramsberg et al., 2012) and CBT (Wu et al., 2020). In addition, research has shown that adding cognitive behavioral therapy (CBT) to TAU (of mostly pharmacological treatment) is more cost-effective compared to TAU alone (Wu et al., 2020). Previous research has also shown that adding an exercise intervention (six weeks of 12 sessions of circuit training) to TAU was cost-effective in youth with depression (Turner et al., 2017). However, very few other MDD interventions have been studied for their cost-effectiveness. Regarding yoga interventions for MDD, to date there are no studies available in which a cost-effectiveness analysis was included. We did find three studies investigating cost-effectiveness of yoga interventions for other conditions. One study found an 8-week yoga intervention to be cost-effective for musculoskeletal conditions in the workplace compared to usual care (Hartfiel et al., 2017), another found a 6-week yoga intervention to be cost-effective compared to self-care advice for employees with low back problems (Aboagye et al., 2015), and a third study found a 12-week yoga intervention to be cost-effective in patients with low back pain compared to usual care (Chuang et al., 2012).

In our randomized controlled trial (registered in the Clinical Trials register with number NCT03388177), we found that adding a mindful yoga intervention (MYI) to treatment as usual (TAU) for young women with depression did not lead to significantly fewer symptoms of depression or fewer diagnosis of MDD at 1-year follow-up (Vollbehr et al., 2022). The aim of the current research is to examine the cost-effectiveness of MYI for young women with MDD. We added this cost-effectiveness study to our RCT.

2. Methods

2.1. Study design

This study was a randomized controlled trial with two conditions (MYI+TAU and TAU). A more detailed description of the design, procedure and assessments has been published elsewhere (Vollbehr et al., 2020). The economic evaluation was performed according to the Dutch guidelines (Healthcare Institution the Netherlands [Zorginstituut Nederland], 2015a) and reported following the Consolidated Health Economic Evaluation Reporting Standards statement (Husereau et al., 2013). Recommendations from the Dutch guidelines were followed regarding using a societal perspective, self-report data, the used costing-approach for informal care and friction period for productivity. The study was conducted in accordance with the principles of the Declaration of Helsinki (version 2013) and the Medical Research involving Human Subjects Act (in Dutch: WMO). All procedures involving human patients were approved by the Medical Ethical Committee of the University Medical Center Groningen (registration number NL.59324.042.16/2016/533).

2.2. Participants and procedure

One-hundred seventy-one women currently in treatment were recruited from January 2017 to October 2018 at psychiatry outpatient clinics in the northern parts of the Netherlands. Inclusion criteria consisted of a primary diagnosis of MDD, age between 18 and 34 years, and the ability to fluently read, write and speak the Dutch language. Exclusion criteria were a current diagnosis of bipolar disorder or substance dependence, current psychotic symptoms, active suicidality, unwillingness or inability to attend nine weekly sessions of yoga, and a current regular yoga practice (average of ≥ 30 min per week over the past six months). Diagnosis was verified and exclusion criteria were assessed using the structured interview for DSM-IV (SCID-I; First et al., 2002) Written informed consent was obtained from all participants.

2.3. Randomization

Randomization using a computerized random number generation process was performed by a methodologist from the Psychology Department of the University of Groningen. Next, treatment allocation was briefed to the contact person (i.e., a clinical psychology student). The contact person then informed the participant about condition assignment. The research assistant conducting the assessments was blind to condition assignment. In case the blinding was broken ($n = 11$), the assessments that were remaining were done by a second rater, not otherwise involved in the study. At the end of the study, fidelity of the blinding procedure was assessed and we found that in less than 50 % of cases the research assistant guessed treatment allocation correctly (resp. 45.9 % [post-intervention], 49.4 % [6-month follow-up], 40.0 % [12-month follow-up]), showing evidence of the adequacy of rater blinding.

2.4. Interventions

We used individualized standard of care (Freedland et al., 2011) according to the Dutch Multidisciplinary Treatment Guideline (Spijker et al., 2012) as TAU. MYI consisted of a manualized 9-week group training with weekly sessions of 1.5-hour. The intervention was designed to change processes involved in depression by enhancing awareness of bodily sensations, emotions and thoughts. The intervention consisted of yoga postures, breathing practices and meditation practices of traditional hatha yoga (Anderson and Sovik, 2000),

combined with instructions designed to increase mindful awareness, and was found to be feasible for participants in a pilot study (Vollbehr et al., 2021). Between the sessions, participants completed an online module that included additional psychoeducation about depression, self-monitoring assignments and practice videos to encourage home practice for approximately 30–45 min a day. MYI was delivered by a psychologist (NKV) who is also a trained yoga teacher (a *Yoga Alliance Registered Yoga Teacher® 500* with over fifteen years of yoga experience and over four years of teaching experience). The intervention was delivered at three psychiatry outpatient clinics and involved 15 groups with a mean of 6 participants per group (range from 3 to 11). The intervention was typically delivered in rooms used for psychomotor therapy or mindfulness interventions. More detailed information about the intervention has been published elsewhere (Vollbehr et al., 2020; Vollbehr et al., 2021).

2.5. Design of the economic evaluation

The economic evaluation focused on the balance between costs and health outcomes of the mindful yoga intervention added to treatment as usual (MYI+TAU) compared to treatment as usual (TAU) in the targeted population. In economic evaluations, costs and health outcomes associated with an intervention are typically used to calculate the incremental cost-effectiveness ratio (ICER) relative to one or more alternatives (Drummond et al., 2005). The formula used for calculating the ICER (with the Depression Anxiety Stress Scales [DASS] as outcome measure) is as follows:

$$ICER = \frac{(C_{MYI} - C_{TAU})}{(DASS_{MYI} - DASS_{TAU})}$$

with C_{MYI} = mean costs in the MYI+TAU group, C_{TAU} = mean costs in the TAU group, $DASS_{MYI}$ = mean DASS difference score in MYI+TAU, and $DASS_{TAU}$ = mean DASS difference score TAU.

The economic evaluation was conducted from a societal perspective; relevant costs within and outside the healthcare sector were prospectively assessed during 15 months for all the included participants. Costs and health outcomes were discounted (1.5 % health outcomes, 4 % costs) in accordance with current Dutch guidelines (Healthcare Institution the Netherlands [Zorginstituut Nederland], 2015a).

2.5.1. Costs

Information on healthcare consumption was collected by means of a detailed case record form (CRF), which was adapted to the context of the current study. The CRF was digitally administered to all the respondents at each of the measurements (baseline, 3 months after baseline, 9 months after baseline, 15 months after baseline). Questions regarding healthcare use and societal costs focused on the previous 3 months at the first and second measurement, and on the previous 6 months at the last two measurement occasions. The CRF assessed, among others, admissions to psychiatric hospitals, contacts with healthcare professionals, medication use, and absence from work. Relevant costs within and outside the healthcare sector were subsequently calculated by combining information on health care consumption and cost prices. Direct MYI costs consisted of costs of contacts between participants and the instructor (hourly wages of €56; 90 min group sessions), materials used during the MYI sessions, development of the online module (including video content), and housing. In addition, costs related to inpatient, semi-inpatient, outpatient, community and informal care, general healthcare, medication use, and productivity losses were assessed. Costs of informal care were based on the monetary valuation of the time invested by relatives or acquaintances in helping or assisting the patient (i.e., household work or visiting healthcare professionals). We used a shadow-price approach for costs of informal care. Out-of-

pocket costs consisted of various types of costs due to health problems that were not included in other aspects of the CRF. These included costs related to cancelled holidays, reduced educational productivity, and other unexpected expenses. Costs of productivity loss due to illness-related absence from work were estimated by means of the friction cost method (Koopmanschap et al., 1995). Furthermore, the costs related to changes in the amount of voluntary (unpaid) work conducted by participants were taken into account.

In order to facilitate comparisons with other economic evaluations, unit prices, i.e., the price of one unit of each included cost type, were mainly based on Dutch standard prices (Healthcare Institution the Netherlands [Zorginstituut Nederland], 2015b). True costs of used resources were estimated when standard prices were not available. All unit prices were based on the price level of the Euro in the year 2019. Reference prices established for previous years were adjusted to prices of 2019 by applying the consumer price index.

2.5.2. Health outcomes

The primary outcome measure of the cost-effectiveness analysis was the Depression Anxiety Stress Scales, short form (DASS-sf; (Lovibond and Lovibond, 1995)), a 21-item self-report questionnaire (scale range 0–3), assessing symptoms of depression, anxiety, and stress. For each group difference, scores were calculated between the last follow-up measurement and baseline. Quality-adjusted life years (QALYs) were used as primary outcome measure for the cost-utility analysis. QALYs were derived from the EQ-5D-5L (Herdman et al., 2011), which is a commonly applied self-administered preference-based instrument. Utilities were calculated by applying the Dutch algorithm (Versteegh et al., 2016). Linear interpolation between time points was assumed when calculating QALYs.

2.6. Statistical analyses

The economic evaluation was conducted alongside a randomized controlled trial, of which the power calculation for the primary outcome measure is provided elsewhere (Vollbehr et al., 2020). This power calculation was based on detecting medium effect size differences (Cohen's $d = 0.5$) on symptoms of depression between the MYI+TAU and the TAU only group. Given that the study was only powered to detect a difference in a depression-related outcome and not in costs, we used probabilistic and medical decision-making techniques to draw inferences about cost-effectiveness.

All analyses were performed based on intention-to-treat. The uncertainty surrounding the incremental cost-effectiveness ratios was assessed by bootstrap analyses (Efron and Tibshirani, 1993). In order to deal with participants for whom not all the data were available at the various measurements, multiple imputation with a bootstrap approach was used (Oostenbrink and Al, 2005). In one of the planned sensitivity analyses, a complete case approach for handling missing data was applied. Incremental cost-effectiveness ratios (ICERs) were calculated for each of the 2500 bootstrap iterations; simulated values of the mean estimates for the cost and outcome differences were added to cost-effectiveness planes (Black, 1990). Cost-effectiveness planes were divided in four quadrants based on the cost- and health-outcomes ratio in the ICER, with the southeast quadrant indicating lower costs and better health outcomes for the MYI+TAU group. Finally, cost-effectiveness acceptability curves (Fenwick et al., 2004) were used to provide information on the probability that MYI is cost-effective compared to TAU for different values a decision maker would be willing to pay for a unit improvement in outcome. Confidence intervals for cost and effect differences were assessed using bootstrap techniques. The analyses were conducted using SPSS (version 25), and CEA-plus (version 2.1).

Table 1
Participants' demographic, clinical and productivity characteristics per group.

Variable	MYI+TAU (n = 88)	TAU (n = 81)
Baseline (T0)		
Age, years, <i>M (SD)</i>	25.25 (4.90)	24.90 (4.36)
Symptoms of depression, <i>M (SD)</i>		
Clinician rated (HDRS) [†]	19.05 (5.78)	18.07 (6.06)
Self-reported (DASS-sf)	21.43 (9.41)	20.57 (9.29)
Number of previous episodes, <i>n (%)</i>		
0	24 (28.9)	29 (36.3)
1–2 episodes	43 (51.8)	34 (42.5)
3 or more	16 (19.3)	17 (21.3)
Duration current episode, <i>n (%)</i>		
2 weeks to 3 months	1 (1.2)	–
3–6 months	10 (12.3)	13 (16.7)
6 months to 1 year	17 (21.0)	9 (11.5)
1–2 years	28 (34.6)	26 (33.3)
2 years or more	25 (30.9)	30 (38.5)
Current treatment duration (months), <i>M (SD)</i>	11.62 (15.46)	11.89 (12.21)
Age of onset first episode, <i>M (SD)</i>	18.11 (5.61)	18.18 (4.88)
Quality of current treatment, <i>M (SD)</i> [‡]	7.19 (1.38)	7.23 (1.06)
Motivation for study, <i>M (SD)</i> [§]	7.92 (0.96)	7.88 (0.95)
Experience with yoga, <i>n (%)</i>		
Yes	24 (27.3)	25 (30.9)
No	64 (72.7)	56 (69.1)
Expecting positive effects of yoga [§] , <i>n (%)</i>	6.02 (1.40)	5.99 (1.35)
Paid work, <i>n (%)</i>	58 (66)	53 (64)
Hours paid work per week, <i>M (SD)</i>	22.6 (11.6)	23.4 (11.3)
Worked less previous 3 months, <i>n (%)</i>	30 (34)	24 (29)
Productivity losses previous 3 months, <i>M (SD)</i>	€2180 (€4616)	€1728 (€4185)

DASS-sf = Depression Anxiety Stress Scales, short form; HDRS = Hamilton

Depression Rating Scale.

[†]n = 83; [‡]scale 1–10; [§]scale 1–9.

Table 2
Mean Costs (€) per participant in and outside the healthcare sector during 15 months.

	MYI+TAU (n = 88)		TAU (n = 83)	
Selection of cost types	Mean costs (SD)	% ¹	Mean costs (SD)	% ¹
<i>Intervention</i>				
MYI	€179 (€39)	100	€0 (€0)	0
<i>(Semi-)inpatient care</i>				
Hospital admissions	€238 (€1.456)	7	€125 (€788)	8
Outpatient clinic visits	€170 (€364)	36	€176 (€430)	37
<i>Outpatient/community care</i>				
Psychiatrist	€275 (€550)	50	€304 (€766)	48
Psychologist	€1.912 (€1.609)	91	€1.577 (€1.745)	78
Group therapy	€351 (€1.076)	24	€225 (€1.100)	25
Social psychiatric nurse	€250 (€875)	15	€278 (€988)	16
PMT	€312 (€1.125)	17	€244 (€1.009)	19
<i>General healthcare</i>				
General practitioner	€156 (€243)	73	€136 (€189)	66
<i>Medication use</i>				
Prescribed medication	€156 (€313)	73	€186 (€328)	66
<i>Outside healthcare sector</i>				
Informal care	€3.089 (€4.230)	64	€3.268 (€6.364)	59
Out-of-pocket costs	€177 (€447)	31	€164 (€426)	30
Productivity loss paid work	€3.105 (€6.801)	35	€4.464 (€11.819)	25

¹Percentage of participants using the cost types concerned.

MYI = mindful yoga intervention; PMT = psychomotor therapy; TAU = treatment as usual.

Table 3
Mean total costs (€) during the study.

Measurement (in months)	MYI+TAU		TAU		Mean cost differences (95 % CI) ²
	Mean total costs	<i>n</i>	Mean total costs	<i>n</i>	
0–3	€3.780	87	€3.282	75	€498 (-€366, €864)
3–9	€5.176	85	€6.046	71	-€870 (-€1.866, €921)
9–15	€2.988	83	€4.468	69	-€1.480 (-€1.630, €138)
0–15 ¹	€11.966	87	€13.818	73	-€1.852 (-€6.611, €2.854)

¹Mean total costs during 15 months, estimates based on the multiple imputation plus bootstrap approach used to account for missing data.

²95 % confidence interval (CI) for the mean cost differences between the groups. Lower and upper boundaries of the CI are presented.

3. Results

3.1. Recruitment and attrition

A complete description of participants' flow has been described elsewhere (Vollbehr et al., 2022). A total of 171 participants were randomized, of whom 88 received the MYI. Baseline assessments of symptoms of depression were completed by all participants and 169 participants completed the demographic characteristics questionnaires. Table 1 shows an overview of the baseline demographic and clinical characteristics of the participants for each group.

3.2. Economic analysis

3.2.1. Costs and healthcare utilization

A selection of the various types of costs (within and outside the healthcare sector) generated by the two groups during four time-intervals of the 15 months of the study are presented in Table 2. Only the most relevant cost types, or those that contributed considerably to the total costs in both groups (≥1 % of total costs), are presented here. These costs are based on the data of participants for whom at least one cost measurement was available during the study (for respondents who did not use specific types of costs or information was missing, €0 was applied when calculating group means for this overview). Furthermore, Table 2 also displays information on the utilization of healthcare services; the percentage of participants using each cost type is provided. Additional information on resource use and cost prices is available on request.

Mean costs directly related to MYI were €179 per patient in the MYI+TAU group. Participants attended 6 offline MYI sessions on

Table 4
DASS outcomes, EQ-5D-5 L (index values), and QALYS during 15 months.

Outcome measure	MYI+TAU		TAU		Mean differences (95 % CI ¹)
	Mean (SD)	N	Mean (SD)	n	
DASS					
T0	67.39 (18.48)	88	69.48 (17.81)	81	-2.10 (-7.62, 3.43)
T1	83.33 (25.12)	87	82.53 (20.40)	76	0.81 (-6.24, 7.85)
T2	90.07 (23.66)	84	89.08 (23.31)	72	0.99 (-6.47, 8.44)
T3	95.88 (22.05)	84	91.80 (25.19)	69	4.08 (-3.57, 11.74)
DASS T0-T3 ²	26.98 (2.39)	87	20.57 (2.88)	73	6.41 (-1.11, 13.74)
EQ-5D-5L					
T0	0.62 (0.18)	88	0.61 (0.20)	81	0.01 (-0.05, 0.07)
T1	0.70 (0.25)	87	0.71 (0.21)	76	-0.01 (-0.08, 0.06)
T2	0.73 (0.22)	85	0.71 (0.24)	72	0.02 (-0.05, 0.10)
T3	0.77 (0.24)	84	0.75 (0.24)	69	0.02 (-0.06, 0.10)
QALY					
T0-T1	0.16 (0.05)	87	0.17 (0.04)	76	0.00 (-0.01, 0.01)
T1-T2	0.36 (0.10)	84	0.35 (0.10)	72	0.00 (-0.03, 0.04)
T2-T3	0.38 (0.10)	82	0.36 (0.11)	68	0.02 (-0.01, 0.05)
QALY T0-T3	0.90 (0.02)	84	0.88 (0.03)	72	0.02 (-0.05, 0.09)

¹95 % confidence interval (CI) for the mean difference between the groups. Lower and upper boundaries of the CI are presented.

²DASS estimated difference scores (based on multiple imputation and bootstrap approach) are presented, calculated as the difference between the last follow-up measurement and baseline. Here, positive difference scores indicate improved functioning.

average, which were provided during the first 9 weeks. In both groups, costs related to care provided by psychologists contributed considerably to the overall costs within the healthcare sector. In this overview, costs within the healthcare sector generally tended to be comparable between groups, for some cost types mean costs were slightly higher for participants in the MYI+TAU group. Outside the healthcare sector, costs related to informal care and productivity loss were high for both groups. Costs of productivity loss related to paid work were substantially lower in the MYI+TAU group.

3.2.2. Total costs

An overview of the mean total costs incurred during the various measurement periods of the study is provided in Table 3. The mean total costs of the MYI+TAU group were (numerically) lower than those of TAU at each measurement, except for the first measurement (0–3 months), however, these differences were statistically not significant. Mean total costs of the 15-month study period were €11.966 for

MYI+TAU and €13.818 for TAU. The differences in mean total costs between groups (-€1.852) were not statistically significant (95 %CI lower boundary -€6.611, upper boundary +€2.854). The absence of significant differences between mean total costs of MYI+TAU and TAU should be interpreted with some caution, since the study was powered (as most economic evaluations) to demonstrate differences in health outcomes and not costs.

3.2.3. Health outcomes

Results of the health outcomes included in the economic analyses are presented in Table 4. Results of the analyses aimed at DASS difference scores and QALYs (derived from the presented EQ-5D-5L values) indicated that there were no differences between the MYI+TAU and TAU groups, although both outcomes tended to be more positive for MYI+TAU (mean DASS difference 6.41, 95 %CI lower boundary -1.11, upper boundary 13.74; mean QALY difference 0.02, 95 %CI lower boundary -0.05, upper boundary 0.09).

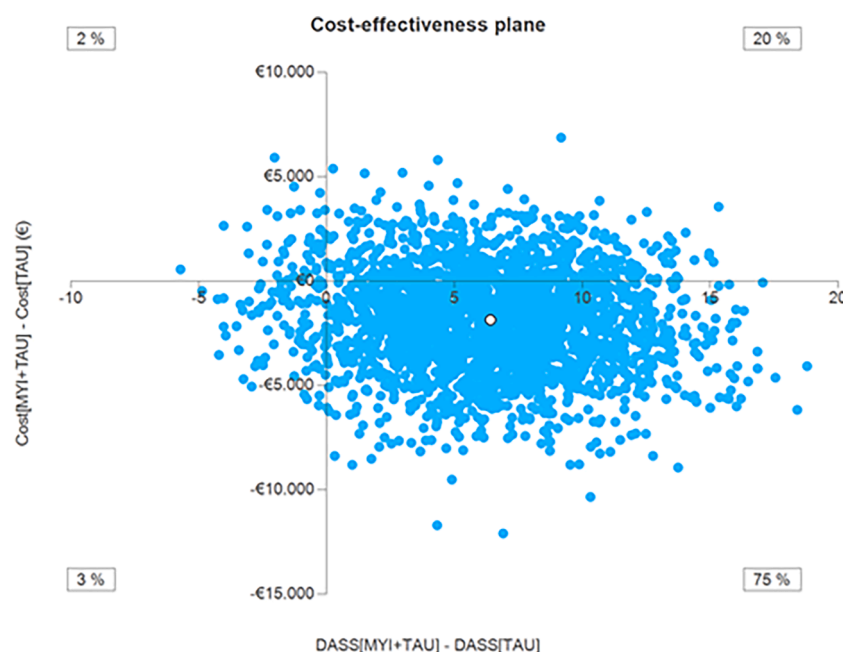


Fig. 1. Cost-effectiveness analyses with DASS as outcome measure.

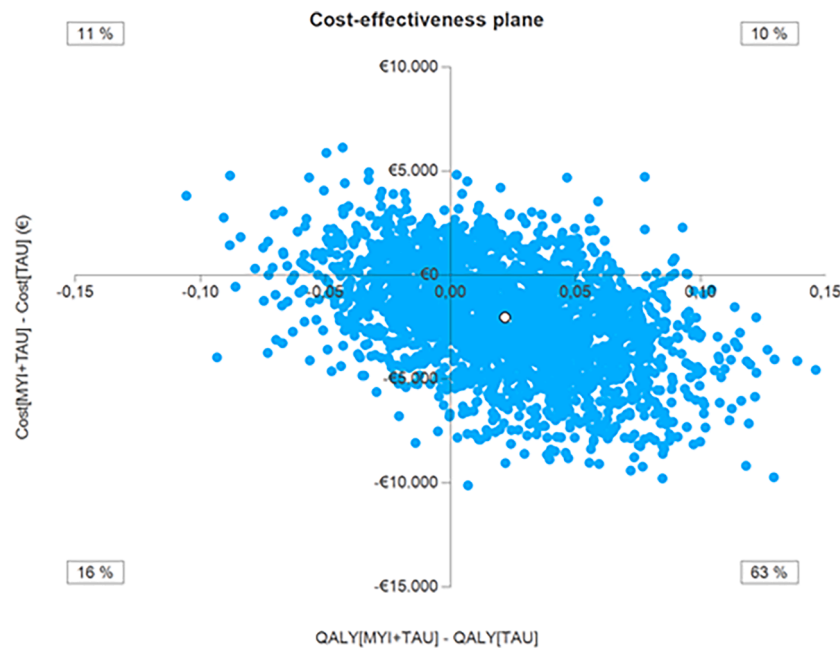


Fig. 2. Cost-effectiveness analyses with QALY as outcome measure.

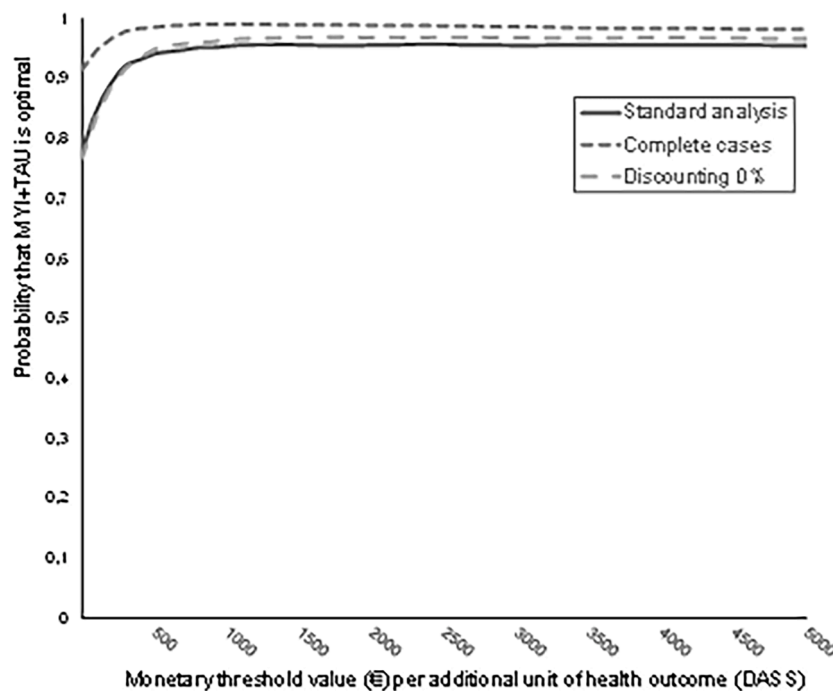


Fig. 3. Cost-effectiveness acceptability curves for the sensitivity analyses.

3.2.4. Cost-effectiveness analysis

The cost-effectiveness analyses are based on data of participants with sufficient available information on both costs and health outcomes (at least 50 % of data available, $n = 160$ [CEA with DASS as primary outcome] and $n = 156$ [CEA with QALY as primary outcome]). Results of the cost-effectiveness analyses with the DASS as primary outcome measure are presented in the cost-effectiveness plane (CEP) in Fig. 1. Results indicated that MYI+TAU was cost-effective compared to TAU alone, with 75 % of the bootstrap simulations located in the southeast quadrant (i.e. lower costs and better health outcomes for MYI+TAU). Results of the CEA analysis with QALYs as primary outcome measure are

presented in Fig. 2. Results indicated that costs were lower and QALY outcomes were better for MYI+TAU, with 63 % of the bootstrap simulations located in the southeast quadrant.

Interpretation of outcomes of cost-effectiveness analyses depends on how much decision-makers are willing to pay for an additional unit of health outcome. Fig. 3 shows the probability that MYI+TAU will be optimal for increasing willingness to pay per additional unit of health outcome (presented for DASS outcomes, standard analysis). Fig. 3 indicates that MYI+TAU is highly likely to be the optimal strategy compared to TAU. The probability that MYI+TAU is optimal starts at 0.78 for a monetary threshold of €0, and further increases for values up

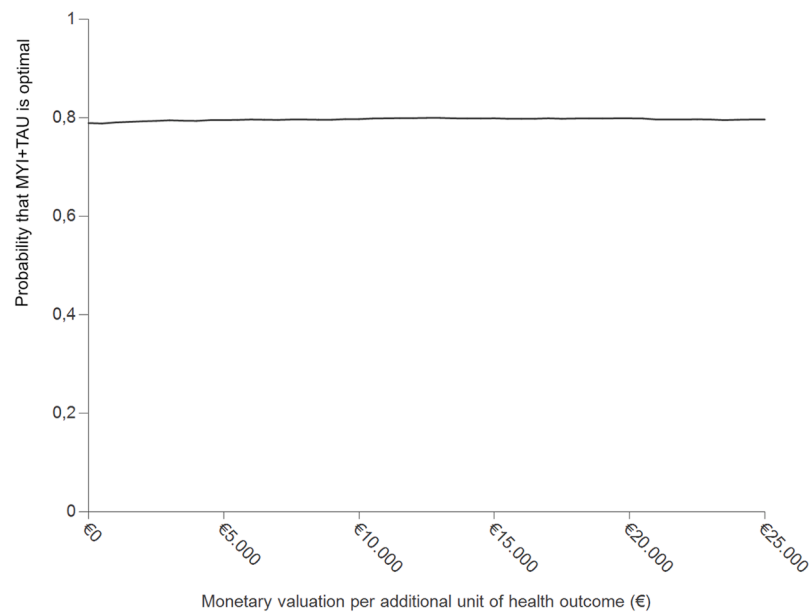


Fig. 4. Cost-effectiveness acceptability curve (with QALY as outcome measure).

to €5000 per additional point gained on the DASS.

Fig. 4 shows the probability that MYI+TAU will be optimal when focusing on QALY outcomes. The probability that MYI+TAU is optimal is approximately 0.79, and is hardly affected by monetary thresholds up to €25,000 per QALY gained.

3.2.5. Sensitivity analyses

In the first sensitivity analysis, a complete case analysis ($n = 146$) was conducted, to compare these results with the applied approach to deal with missing data in the standard analysis. Fig. 3 shows that the complete case analysis is associated with a higher probability of MYI+TAU being optimal than the standard analysis.

Since there is no international consensus on the inclusion, scope, and valuation of the costs of invested time in cost-effectiveness analysis, these costs were not included in the standard analysis. We did include these in the second sensitivity analysis. Guidelines in the Netherlands suggest to only assess time costs related to the intervention under study when invested time directly affects paid work. These average time costs were estimated at €125 per respondent in the MYI+TAU group, which likely overestimated true time costs since we ignored the fact that most participants worked parttime (which could be associated with lower actual time costs due to more flexible working hours). The results of this analysis in Fig. 3 show that overall outcomes are still in favor of MYI+TAU, with only a slightly lower probability of cost-effectiveness for MYI+TAU for threshold values up to €500.

The third sensitivity analysis focused on the influence of discounting. Fig. 3 presents the acceptability curves for the standard analysis and the described sensitivity analyses. Applying zero discount rates for costs and health outcomes only has a minimal impact on overall outcomes.

3.2.6. Missing data

Although advanced methodology was used to handle missing data, the data of 11 (6 %) of the initially included 171 respondents were insufficient and could not be included in the main cost-effectiveness analyses. Of these 11 respondents, 1 was randomized to the MYI+TAU group, and 10 to TAU. In order to gain insight in the characteristics of respondents with substantial missing data, comparisons were made between these and the other respondents. When focusing on baseline outcomes that were relevant for the economic analyses, i.e., societal costs, DASS scores, and QALYs, no statistically significant differences were found between respondents with substantial missing data and the

other respondents. Mean societal costs during the 3 months before T0 were €3422 for respondents with substantial missing data, and €4889 for the other respondents. In terms of health outcomes, mean DASS scores were slightly worse (mean difference -3.9 , 95 % CI $-11.6, 3.7$), and mean QALY outcomes during the previous 3 months were lower (mean difference -0.03 , 95 % CI $-0.06, 0.01$) for respondents with substantial missing data.

4. Discussion

In spite of several limitations that we address below, results of the economic analyses gave some indication that MYI+TAU was likely to be cost-effective compared to TAU in the studied population. In particular, during the 15 months of the study, the costs of productivity loss due to absence from paid work were substantially lower in the MYI+TAU group compared to the TAU group. Since both groups seemed comparable in terms of paid work characteristics at baseline (and costs of productivity losses were slightly higher in MYI+TAU before baseline), it seems plausible that the MYI intervention had a direct impact on the (reduced) costs of productivity losses in the MYI+TAU group. The duration of absence was shorter in the MYI condition, which seems to be related to the health improvement in the MYI condition.

Mean total societal costs during the 15 months of the study were €11.966 for the MYI+TAU group and €13.818 for the TAU group. Health outcomes (DASS and QALY) were slightly in favour of MYI+TAU. However, differences between groups in terms of mean total costs and health outcomes were not statistically significant. Combining costs and health outcomes in cost-effectiveness analyses indicated that there is a high probability that MYI+TAU is cost-effective compared to TAU. Results of the various sensitivity analyses also supported this conclusion. As noted above, the treatment outcome results of this trial indicated that adding MYI to TAU for young women with MDD did not lead to fewer depression symptoms (Vollbehr et al., 2022). However, by jointly analyzing health outcomes and societal costs, the cost-effectiveness analyses provided important additional information for decision-makers, and demonstrated that adding MYI to TAU is likely to be cost-effective. In this light it is important to note that the total costs of the MYI-intervention were relatively low (€179 per patient).

Although advanced methodology was used to handle missing data, the data of 6 % of the respondents were considered insufficient to be included in the main cost-effectiveness analyses. When comparing

respondents with substantial missing data to the other respondents, mean societal costs before the start of the study were lower, and health outcomes (in particular QALYs) seemed worse. Although these differences were not statistically significant, the size of the differences did seem relevant. The interpretation of this finding is not straightforward. It might be that the condition of these respondents worsened shortly before the start of the study, which was not yet reflected in societal costs during the previous 3 months. Perhaps more importantly, 10 out of the 11 respondents with substantial missing data were in the TAU group, despite the followed randomization procedure. A possible explanation could be that these 10 respondents would have preferred to be in the experimental condition, and combined with their seemingly worse health status at the beginning of the study, this might have lowered their motivation to continue in the study. The potential consequences of the differential drop-out rates between the two conditions for the overall results of the study seem limited, especially since differences between substantial missing data respondents and the other respondents were not statistically significant. It seems important to at least acknowledge (and perhaps find ways to prevent) that some respondents in control conditions of studies focusing on MYI, might be prone to prematurely discontinue these studies.

Given that we only found three trials studying cost-effectiveness of yoga interventions, all in patients with somatic conditions, of which none included a population of patients with mental health problems such as MDD, we have rather limited information to compare our results with. However, our findings are generally in line with the positive findings regarding cost-effectiveness of yoga interventions compared to usual care for different conditions including musculoskeletal conditions in the workplace (Hartfiel et al., 2017), employees with low back problems (Aboagye et al., 2015), and patients with low back pain (Chuang et al., 2012).

When we compare the societal costs in our trial to another recent trial conducted in the Netherlands for patients with MDD that examined the cost-effectiveness of adding preventive cognitive therapy (PCT) to antidepressant maintenance (Klein et al., 2019), the results indicated that the mean total costs of the PCT group were €6.814 and of the antidepressant group were €10.264 over 24 months. In our study the total costs were €11.966 for the MYI+TAU group and €13.818 for the TAU group over 15 months. This difference in costs might be due to the fact that participants in the trial of Klein et al. were all in remission of MDD, not having an actual diagnosis of MDD at the start of the trial, where in our study all participants were having a diagnosis of MDD at the start of the trial. Therefore, TAU in our study consisted of quite an extensive form of treatment, with a large number of participants receiving medication (45.9%), a majority of participants (51.8%) receiving more than one form of TAU, and receiving a rather high number of mean sessions (Vollbehr et al., 2022), whereas TAU in the PCT study consisted of maintenance of antidepressants only (Klein et al., 2019). Finally, in our study 26% (MYI+TAU) and 32% (TAU) of the total costs were due to productivity loss. This is in line with a review (Krol et al., 2011) showing that in depression a large share of the societal costs is due to productivity loss. According to this review, on average 60% of societal costs is due to productivity losses in studies aimed at depression, with large variations between studies due to differences in applied costing methods.

4.1. Limitations

Several limitations of our study need to be addressed. First, the power analysis of our study was based on the clinical outcome measure that was considered most relevant in the current context (DASS). Therefore, as in most cost-effectiveness studies, our study was not powered to detect significant differences regarding outcomes typically used in economic analyses, like QALYs and costs. We used probabilistic techniques and sensitivity analyses to make estimations of the cost-effectiveness and cost-utility. Second, it may be difficult to compare current economic findings directly to other healthcare systems, not only

due to substantial differences between healthcare systems, such as differences in TAU, but also to (international) variations in methodology used for economic analyses. Another limitation is the possibility of a recall bias, which is often present in cost-effectiveness analyses, as participants are asked to recall healthcare use over a longer period of time (in our study the longest period was 6 months; (Evans and Popova, 2016). Although we asked our participants to use a diary during the study period and use this diary when completing the questionnaires, we cannot rule out that the total costs in the study might have been underestimated (Evans and Popova, 2016; van den Brink et al., 2004). As our CEA was conducted alongside a randomized controlled trial, this might have reduced the influence of recall bias on our results, as both groups are expected to have the same amount of recall bias.

Finally, the generalizability of our findings may be limited to young women with depression only, as we did not take men or older adults into account. Research has found different effects of meditation interventions for men and women (Rojiani et al., 2017), and that psychotherapeutic interventions have larger effects in adults compared to adolescents (Cuijpers et al., 2020). Therefore, it is important to note that our findings are not readily generalizable to other populations than young women with depression.

4.2. Recommendations for clinical practice and future research

The current finding that adding MYI to TAU is likely to be cost-effective in this population suggests that MYI can be a beneficial addition to the available treatment options in this group from an economic perspective. We recommend future studies investigating the effectiveness of mindful yoga interventions to include a cost-effectiveness analysis, so more information can become available to policy makers about potential benefits regarding reductions in individual suffering as well as societal costs.

CRedit authorship contribution statement

Nina K. Vollbehr: Conceptualization, Writing – original draft. **A. Dennis Stant:** Conceptualization, Formal analysis, Investigation, Methodology, Writing – review & editing. **H.J. Rogier Hoenders:** Conceptualization, Supervision, Writing – review & editing. **Agna A. Bartels-Velthuis:** Conceptualization, Supervision, Writing – review & editing. **Maaïke H. Nauta:** Conceptualization, Writing – review & editing. **Stynke Castelein:** Conceptualization, Writing – review & editing. **Maya J. Schroevers:** Conceptualization, Writing – review & editing. **Peter J. de Jong:** Conceptualization, Writing – review & editing. **Brian D. Ostafin:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgements

The authors would like to thank Petri Engelen for her involvement in the study, including participant recruitment and assessments. The authors are deeply grateful to all 171 women for participating in this study.

Ethical considerations

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation. The study was conducted in accordance with the principles of the Declaration of Helsinki (version 2013) and the Medical Research involving Human Subjects Act (in Dutch: WMO). All procedures involving human patients were approved by the Medical Ethical Committee of the University Medical Center

Groningen (registration number NL.59324.042.16/2016/533). Informed consent was obtained from all participants before inclusion in the study.

Funding

We gratefully acknowledge funding from ZonMw (grant number 636110004), Lentis Psychiatric Institute, the Triodos Foundation and the Mind & Life Europe Foundation (grant number #2015-EVarela-Vollbehr, Nina).

Data availability

The data that support the findings of this study are available on request from the corresponding author, NKV. The data are not publicly available due to their containing information that could compromise the privacy of the research participants.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.psychres.2023.115692](https://doi.org/10.1016/j.psychres.2023.115692).

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