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Business case for psychosocial interventions in clinics: potential for decrease in treatment discontinuation and costs

BIOGRAPHY

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KEY MESSAGE

This proof-of-concept business case may help decision makers determine rationally whether cognitive behavioural therapy or mindfulness is worth implementing alongside fertility treatment services. The added value of these psychosocial interventions may include less anxiety and depressive symptoms, higher quality of life and pregnancy rate, lower discontinuation rates, and cost savings.

ABSTRACT

Research question: From a value-based healthcare (VBHC) perspective, does an assessment of clinical outcomes and intervention costs indicate that providing cognitive behavioural therapy (CBT) or mindfulness to women seeking fertility treatment add value compared with no such intervention?

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Declaration: AAK, JCH, GvdD, MS, JS, JL, AH, and JB have received consulting or advisory fees from Ferring BV; LMvW and NT were employed by Ferring BV at the time of this study; ES is employed by Ferring BV; HD and MT are employed by KPMG Health, which received consulting fees from Ferring BV; HD is also employed by Delft University Technology; JS has received financial support or fees from Ferring BV; Merck BV and Goodlife; JL has received financial support or fees from Merck, Ferring BV and Gedeon Richter, and has served on a Data Safety Monitoring Board or Advisory Board for the LOCI Trial UK; JL serves as the president of the AE PCOS Society; JCH has received consulting or speaker fees from Haleon, Flo, Adora, Gedeon Richter, Cook Medical, and Theramex; JCH is the author of a book, 'Your Fertile Years'; JB has received financial support or fees from ESHRE, Ferring Pharmaceuticals A/S and Ferring Arzneimittel GmbH, and Merck Serono Ltd and Merck Group; JB is employed by Cardiff University, which holds IP rights to Treatment Planning and Continuation Intervention, Positive Reappraisal Coping Intervention, and the Emotion Tracking Tool; JB reports a relationship with Psych-Fertility Consulting Ltd.

KEYWORDS

business case
value-based health care
psychosocial interventions
fertility treatment
cognitive behavioural therapy
mindfulness

Design: Proof-of-concept business case based on a VBHC perspective that considers clinical outcomes and costs. Potential effects on psychological and fertility outcomes were based on existing research. Cost outcomes were estimated with a costing model for the Dutch fertility treatment setting.

Results: Thirty-two studies were identified; 13 were included. Women who received CBT had 12% lower anxiety, 40% lower depression and 6% higher fertility quality of life; difference in clinical pregnancy rates was six percentage points (CBT [30.2%]; control [24.2%]); difference in fertility discontinuation rates was 10 percentage points (CBT [5.5%]; control [15.2%]). Women who received training in mindfulness had 8% lower anxiety, 45% lower depression and 21% higher fertility quality of life; difference in mean clinical pregnancy rate was 19 percentage points (mindfulness [44.8%]; control [26.0%]). Potential total cost savings was about €1.2 million per year if CBT was provided and €11 million if mindfulness was provided. Corresponding return on investment for CBT was 30.7%, and for mindfulness 288%. Potential cost benefits are influenced by the assumed clinical pregnancy rates; such data related to mindfulness were limited to one study.

Conclusions: The provision of CBT or mindfulness to women seeking fertility treatment could add value. Higher quality primary studies are needed on the effect of mindfulness on clinical pregnancy rates.

INTRODUCTION

Infertility is a biopsychosocial phenomenon that negatively affects the quality of life and wellbeing of people experiencing it. At the time of diagnosis, psychological consequences may include feelings of sadness, envy, depression, fear, worry, and shame (*Payne et al., 2021*; *Boivin et al., 2022*; *2023*; *Nik Hazlina et al., 2022*). During the course of fertility treatment, other feelings such as lower self-esteem, anger, isolation, hopelessness and inadequacy, and low confidence may arise (*Payne et al., 2021*; *Boivin et al., 2022*; *2023*). Disruption of daily life activities, such as work, has also been reported (*Boivin et al., 2022*). Psychological distress can arise from treatment-related factors, such as the stringent timeline, medical constraints, financial burden, and uncertainty (*Sax and Lawson, 2022*). Social consequences are considerable, and may include relational problems, including intimate partner violence, sexual dysfunction, social isolation and ostracism, stigma, sense of loss, and sense of loss of identity (*Payne et al., 2021*; *Lancet Global Health, 2022*; *Sater et al., 2022*; *Wang et al., 2022*). A recent study indicated that women seeking fertility treatment rated infertility to be a greater life stressor than the COVID-19 pandemic (*Vaughan et al., 2020*).

Furthermore, the way fertility treatment providers interact and communicate can also be a source of stress and anxiety for women (*Gameiro et al., 2015*). Psychosocial issues and insufficient professional support with managing these problems may be reasons why women discontinue fertility treatment (*Gameiro et al., 2012*; *Chauhan et al., 2021*). In parallel, research indicates that fertility treatment providers feel ill-equipped to provide adequate communication and counselling (*Boivin et al., 2017*). These reciprocal influences between women and providers, which underscore an unmet need for professional psychosocial services in fertility treatment centres, need to be acknowledged.

The seeking, provision, and funding of psychosocial interventions during fertility treatment is inconsistent around the world (*Blyth, 2012*; *Morshed-Behbahani et al., 2020*; *Payne et al., 2021*; *Boivin et al., 2022*). In the USA and UK, only 12% of fertility clinics offer integrated psychological programmes (*Raad et al., 2022*). Clearly, a paradigm shift to integrated fertility treatment in which staff at fertility clinics are equipped to respond adequately to psychosocial issues is a priority (*Boivin and Gameiro, 2015*; *Gameiro et al., 2015*). Failure to do so may negatively affect the overall performance of fertility clinics (*Sax and Lawson, 2022*).

A barrier to embedding psychosocial treatment into fertility care may be the lack of studies integrating clinical and financial data into a business case. Business cases may provide fertility-treatment stakeholders and decision makers with more complete information and insight into how to improve delivery of care. That is, is it worthwhile investing funds into a new service?

From a value-based healthcare (VBHC) perspective, a new service may be considered worth implementing in practice if it generates 'value' for the patient in the form of improved patient-relevant health outcomes, and the total treatment costs to achieve the given outcomes remain the same or are reduced (*Porter, 2009*; *Teisberg et al., 2020*). Patient-relevant outcomes include those that measure change in terms of capability or function ('ability of patients to do the things that define them as individuals and enable them to be themselves'), comfort ('relief from physical and emotional suffering', such as anxiety and distress), and calm ('ability to live normally while getting care' and 'freedom from the chaos [experienced] in the healthcare delivery system') (*Teisberg et al., 2020*). Common patient-reported outcomes in the infertility setting are anxiety, depression and fertility quality of life (*Kitchen et al., 2017*; *Austin et al., 2020*). By focusing on improving health outcomes relative to costs rather than costs alone, VBHC aligns the interests of patients and clinicians to address what matters to both. This approach encourages stakeholders to consider how healthcare delivery could be optimized (*Teisberg et al., 2020*).

To date, a number of reviews investigating the effect of psychological therapy approaches such as cognitive behavioural therapy (CBT), mindfulness, counselling, and acceptance and commitment therapy on psychological and clinical outcomes, have been conducted (*Katyal et al. 2021*; *Zhou et al., 2021*; *Dube et al., 2023*; *Ha et al., 2023*; *Kremer et al., 2023*; *Warne et al., 2023*), including an umbrella review (*Paraskevi et al., 2021*). Findings from these reviews indicate that psychosocial interventions may have favourable effects on fertility stress, anxiety, distress, improved fertility quality of life, and pregnancy rate; however, the results are not consistent (*Katyal et al. 2021*; *Paraskevi et al., 2021*; *Zhou et al., 2021*; *Dube et al., 2023*; *Ha et al., 2023*; *Kremer et al., 2023*; *Warne et al., 2023*). A high risk of bias and heterogeneity in, for example, study design, and the interventions themselves, are two of the main methodological issues identified in these

reviews and clinical guidelines (*Gameiro et al., 2015*; *Paraskevi et al., 2021*; *Dube et al., 2023*; *Kremer et al., 2023*). Nevertheless, CBT and mindfulness are commonly used in healthcare settings, including infertility. Briefly, CBT aims to improve coping skills and reduce infertility- and treatment-related stress, anxiety, depression, and self-criticism by teaching the individual how to change unhelpful thinking, behavioural patterns, or both, through cognitive restructuring and behavioural techniques (*American Psychological Association, 2018a*). Mindfulness pertains to becoming '[aware] of one's internal states and surroundings', and teaches individuals to become aware of one's emotional, cognitive and physical self (mind–body) in the present moment without reacting to or judging them. The awareness gained potentially improves emotional regulation in health situations (*American Psychological Association, 2018b*).

The aim of the present study was to present a business case for providing either CBT or mindfulness training to women seeking fertility treatment compared with no such intervention on psychosocial, clinical and cost outcomes. The research question of this proof-of-concept study was as follows: from a VBHC perspective, does an assessment of clinical outcomes and intervention costs indicate that providing CBT or mindfulness to women seeking fertility treatment adds value compared with no such intervention?

MATERIALS AND METHODS

This proof-of-concept study involved two general steps: identifying and extracting relevant data on clinical outcomes from published research, and estimating the changes in costs using a costing model created in Microsoft Excel (version 2108).

Identification of studies for modelling

To identify relevant studies reporting psychosocial and fertility outcomes after CBT or mindfulness, a scoping literature review was conducted. Searches were conducted in *Embase, PubMed, Web of Science, Cochrane Library, Emcare, PsycINFO* and *Academic Search Premier*. The search period was from inception date of the respective databases to October 2022. Key words included cognitive behavioural therapy, problem-solving therapy or mindfulness, and infertility, fertility, fertility treatment or reproductive techniques. Problem-solving therapy was included as a key word because it is also a cognitive behavioural intervention and, in practice, shares similar elements with CBT (*Warmerdam et al., 2010*).

Study inclusion criteria were as follows: use of a controlled study design, (randomised controlled trial or non-randomised controls); women receiving assisted reproductive technology (ART); data on at least one relevant psychosocial or fertility outcome; and the evaluated interventions were either a CBT intervention (CBT or problem-solving therapy), or a mindfulness intervention, but not a mixture of these categories. To ensure a sufficient pool of articles, studies in which the interventions were supplemented with relaxation techniques were included. The description of the intervention in each potential article was screened by two of the co-authors who are experts in health psychology (JB, AAK).

Exclusion criteria were as follows: studies without a control group or based on secondary data; study population did not include women being treated for their first cycle of ART or included women who were not yet pregnant; no data on relevant psychosocial or fertility outcomes that could be extracted or converted; the evaluated intervention was not clearly based on either CBT or mindfulness but a combination of elements included medication or had another focus such as, for example, stress reduction, coping skills, providing information, partnership therapy, music therapy, writing therapy, or hypnosis; or duplicate publications.

Psychosocial and fertility outcome definitions for modelling

Relevant psychosocial outcomes were defined as anxiety measured by the State Anxiety scale of the State-Trait Anxiety Inventory (20 items) (*Spielberger et al., 1983*); depression as measured by the Beck Depression Index (21 items) (*Beck et al., 1961*); and fertility quality of life measured by the FertiQoL (core FertiQoL: 24 items) (*Boivin et al., 2011a*). The relevant fertility outcomes were clinical pregnancy rate or treatment discontinuation. Clinical pregnancy rate was defined as pregnancy in a patient (patient unit of analysis) confirmed by ultrasound visualisation of fetal sac or heartbeat (*Zegers-Hochschild et al, 2009*). Discontinuation of fertility treatment was defined as a patient not starting ART as scheduled or not starting another cycle within 12 months after a failed first cycle (*Gameiro et al., 2013*).

Data extraction from included studies for modelling

For each psychosocial outcome (anxiety, depression and fertility quality of life) pre- and post-intervention numerical scores from the included studies were extracted, and the percent change was calculated from the mean data presented in each study using the formula (post-intervention score − pre-intervention score)/pre-intervention score. Data were then summarised in a radar chart (*Thaker et al., 2016*). When data from more than one study were available, the change attributable to the psychosocial intervention was calculated using weighted means. When disaggregated FertiQoL data were reported, Core FertiQoL scores were calculated for relevant studies by summing the scores of the emotional, mind–body, relational and social subscales, and dividing by 4.

For fertility outcomes (clinical pregnancy rate, fertility treatment discontinuation rate), which were expressed in percentages, the mean or weighted mean differences were calculated between the intervention versus control group after the intervention period. The difference between the groups, that is, the difference attributable to the given intervention, was defined as the difference in percentage points. The percentage point differences were also summarised in a radar chart.

Costing model

To estimate the difference in fertility treatment costs attributable to either CBT or mindfulness, a costing model was created in Microsoft Excel based on an adaptation of the model reported by *Steegers-Theunissen et al. (2020)*. The structure of the model is presented in **Supplementary Figure 1**, and an overview of the model parameters and data sources are provided in **Supplementary Table 2**. All costs were reported in 2021 Euros.

The Dutch healthcare system was chosen as the setting for this comparative evaluation. In The Netherlands, the use of patient-relevant outcomes to determine the value of health care has been receiving greater attention in Dutch health policy since 2018 (*Ministerie van Volksgezondheid, Welzijn en Sport, 2018*). Infertility affects approximately one in 10 Dutch women (*Boivin et al., 2007*). If a medical reason exists for infertility, basic

health insurance covers three treatment cycles of intracytoplasmic sperm injection (ICSI) or IVF, with or without past intrauterine insemination (IUI) or ovulation induction. The Netherlands has approximately 40 fertility clinics, and the provision and type of psychosocial support are not standardised.

To determine the potential effect of psychosocial support on the costs of fertility treatment, the target population included Dutch women aged between 25 and 44 years and undergoing their first cycle of ART (IUI, IVF and ICSI). On the basis of prevalence and incidence data, the number of women eligible for a first cycle of ART annually was estimated to be 38,432 women (*Steures et al., 2006*; *Van Asselt et al., 2010*; *deGynaecoloog, 2022*).

Cost data on fertility treatment (IUI, IVF and ICSI) were collected from databases of published research, expert opinion and publicly available data, such as the Open Data DIS database of the Dutch Healthcare Authority (*Nederlandse Zorgautoriteit, 2022*). The costs of CBT and mindfulness were based on the delivery format from the online Mental Stark platform, which offers psychosocial support to women seeking fertility treatment (*Mental Stark, 2022*). The Mental Stark programme is a self-administered online programme, with additional chat function with a professional and stepped-up care in the form of optional face-to-face support. An assumption was made that psychosocial support would be provided in a digital format (a website application consisting of modules) for a duration of 6 months to allow sufficient time to use the platform, including any optional counselling. The percentage of women accepting psychosocial support when offered (28%) was based on uptake data from a randomised controlled trial conducted in the Netherlands (*Ockhuijsen et al., 2014*). Because the optional in-person counselling sessions may be requested to supplement the digital format of the interventions, an estimate of costs was also calculated for this scenario. On the basis of data provided by Mental Stark, the following parameters were used: for CBT, 15% of patients participated in two counselling sessions; and for mindfulness, 15% participated in one counselling session (personal communication). When data were unavailable, values were estimated using assumptions that were validated by experts in infertility treatment, i.e. (gynaecologists, reproductive science and fertility specialists, medical and health psychologists).

The following costs were estimated: fertility treatment costs per woman or couple, and for the total target group, when women seeking fertility treatment receive CBT or mindfulness compared with when they do not. A positive difference in costs indicated that total fertility treatment cost savings were made when a psychosocial intervention was provided, and a negative difference indicated additional costs. In addition, the return on investment (ROI) of each psychosocial intervention was calculated. Return on investment evaluates the efficiency of the psychosocial intervention in its financial investment. It is an indicator of whether the intervention's benefits compare favourably to its costs and can be greater than 100%. Return on investment was calculated using the following equation:

$$ROI = \left\{ \frac{\Delta \ costs\ of\ fertility\ treatment}{costs\ intervention} * 100\% \right\} - 100\%$$

The findings of the ROI calculations were also summarised, together with the clinical outcomes in a radar chart (*Thaker et al., 2016*). Furthermore, one-way sensitivity analyses were conducted to gain insight into how the difference in total fertility costs attributable to a given psychosocial intervention may vary depending on the rate of women accepting psychosocial support when offered and clinical pregnancy rate. An overview of the parameters tested in the sensitivity analysis is presented in **Supplementary Table 2**.

RESULTS

Difference in psychosocial and fertility outcomes

A total of 32 potential studies with a randomised controlled trial or non-randomised control trial design were identified. Of these, 13 studies (eight pertaining to CBT and five to mindfulness) were included, and their general characteristics are presented in TABLE 1. Excluded studies and reasons for exclusion are presented in **Supplementary Table 3**.

Psychosocial outcomes for CBT and mindfulness are presented in TABLE 2. The difference between pre- and post-scores indicated that anxiety and depression were lower and quality of life higher in those who received the intervention. Cognitive behavioural therapy reduced anxiety scores by 12% (*Kim et al., 2014*; *Domar et al., 2015*) and depression by 40% (*McNaughton-Cassill et al., 2002*; *Faramarzi et al., 2008*; *Gojani et al., 2018*), and increased fertility quality of life scores by 6% (*Domar et al., 2015*; *Heredia et al., 2020*). Mindfulness reduced anxiety scores by 8% (*Chan et al., 2012*; *Galhardo et al., 2013*) and depression by 45% (*Galhardo et al., 2013*; *Nery et al., 2019*; *Kalhori et al., 2020*), and increased fertility quality of life scores by 21% (*Li et al., 2016*).

Fertility outcomes are presented in TABLE 3. Three studies (*Haemmerli et al., 2010*; *Gorayeb et al., 2012*; *Domar et al., 2015*) that evaluated the effect of CBT on clinical pregnancy rate were identified and one study (*Li et al., 2016*) for mindfulness. The difference in weighted mean clinical pregnancy rate was six percentage points in women who received CBT (30.2%) compared with those who did not (24.2%). The difference in mean clinical pregnancy rate was 19 percentage points in women who received training in mindfulness (44.8%) compared with women who did not (26.0%). With the effect of CBT on rates of discontinuing fertility treatment, one study reported that discontinuation rates differed by 10 percentage points among those who received the intervention (5.5%) versus those who did not (15.2%) (*Domar et al., 2015*). No studies reporting the effect of mindfulness on this outcome were identified.

Difference in fertility care costs

The potential cost savings of cost benefit ratio per woman or couple were €31 if women received CBT during fertility treatment, corresponding to an estimated €1.2 million total cost savings for the Dutch healthcare system and a ROI of 30.7%. Mindfulness was associated with a potential cost savings of €291 per woman or couple, which corresponded to estimated total cost savings for the Dutch healthcare system of €11 million and a return on investment of 288%. The main cost driver affecting the estimate of cost savings is the difference in clinical pregnancy rate attributable to the psychosocial intervention.

When the additional intervention costs for in-person counselling sessions were included, CBT was no longer associated with cost savings per woman or couple (€0). Also, the potential cost savings per woman or couple for mindfulness

TABLE 1 GENERAL CHARACTERISTICS OF THE INCLUDED STUDIES AND BRIEF DESCRIPTION OF EVALUATED INTERVENTION

Intervention	Study (year)	Clinical outcomes evaluated	Study design	Country	Intervention group, *n*	Control group, *n*	Description of the intervention
CBT	*Domar* et al. *(2015)*	Anxiety, fertility quality of life, clinical pregnancy rate, discontinuation rate of fertility treatment	RCT, single centre	USA	89	77	Self-administered programme consisting of cognitive and relaxation components that followed a prescribed sequence that aligned with different stages of fertility treatment, i.e. stimulation and waiting stage.
	Faramarzi et al. *(2008)*	Depression	RCT, single centre	Iran	42	40	Weekly 2-h sessions over a 10-week period; sessions five to 10 included the addition of progressive muscle relaxation.
	Gojani et al. *(2018)*	Depression	RCT, single centre	Iran	PRCI: 36 PSS: 36	36	PRCI: two group training sessions and twice daily repetition of the 10 positive thought cards during waiting stage; PSS: three group training sessions and implementation during the waiting stage.
	Gorayeb et al. *(2012)*	Clinical pregnancy rate	RCT, single centre	Brazil	93[a]	95[a]	Five weekly 2-h group sessions for couples.
	Haemmerli et al. *(2010)*	Clinical pregnancy rate	RCT, single centre[b]	Switzerland	60	64	Eight-week, internet-based CBT programme.
	Heredia et al. *(2020)*	Fertility quality of life	RCT, single centre	Spain	23	23	One individual 90-min session.
	Kim et al. *(2014)*	Anxiety	Non-RCT, single centre	South Korea	26	24	Five 2-h group sessions over a 5-week period supplemented by text messages, emails and phone calls at least twice a week when needed.
	McNaughton-Cassill et al. *(2002)*	Depression	Non-RCT, single centre	USA	26[a]	19[a]	Group sessions of 1.5 h for couples, twice a week during the 3-week period of undergoing IVF treatment.
Mindfulness	*Chan* et al. *(2012)*	Anxiety	RCT, single centre	China	172	167	Four 3-h group sessions over a 4-week period
	Galhardo et al. *(2013)*	Anxiety, depression	Non-RCT, multicentre	Portugal	55	37	Ten 2-h group sessions over a 10-week period; spouses are invited to participate in three of the 10 sessions.
	Kalhori et al. *(2020)*	Depression	RCT, single centre	Iran	45	45	Eight 90-min group sessions, where two sessions were followed per week.
	Li et al. *(2016)*	Fertility quality of life, clinical pregnancy rate	Non-RCT, single centre	China	58	50	Six 2- to 2.5-h group sessions over a 6-week period.
	Nery et al. *(2019)*	Depression	RCT, single centre	Brazil	62	37	Eight 2-h group sessions over an 8-week period.

[a] Number of women among the couples who participated in either group.

[b] Organised and conducted from a single centre in Switzerland; however, participants were located in six different countries, with most living in Switzerland.

CBT, cognitive behavioural therapy; h, hour; n, number of participants; non-RCT, non-randomised controlled trial; NR, not reported; PRCI, positive reappraisal coping intervention; PROM, patient-reported outcome measure; PSS, problem-solving skills; RCT, randomised controlled trial.

decreased to €266 (**Supplementary Figure 2**).

Radar chart

The value of providing CBT or mindfulness to women seeking fertility treatment in terms of psychosocial, fertility and cost outcomes is presented in a radar chart (FIGURE 1**)**.

Sensitivity analyses

The sensitivity analyses of CBT indicated that a lower adoption rate of 25% changed the cost savings to €18 per woman or couple and an adoption rate of 31% to €45 per woman or couple. The assumption of lower clinical pregnancy rate (1% versus 6% in the main analysis) led to extra costs of €68 per woman or couple.

In evaluating mindfulness, the lower adoption rate (25%) resulted in cost savings per woman or couple but a lower amount (€252), and the higher adoption rate (31%), a higher amount (€330). A lower clinical pregnancy rate of 5% indicated no cost savings but extra costs of €3 per woman or couple (FIGURE 2**)**.

TABLE 2 STUDIES ON CHANGES IN ANXIETY, DEPRESSION AND QUALITY OF LIFE SCORES AMONG WOMEN WHO RECEIVED EITHER COGNITIVE BEHAVIOURAL THERAPY OR TRAINING IN MINDFULNESS DURING FERTILITY TREATMENT

Intervention	Outcome evaluated (PROM used)	Study (year)	Sample size intervention group, *n*	Mean score at baseline (SD)	Mean score after intervention (SD)	Weighted mean score at baseline	Weighted mean score after intervention	Mean change	% improvement
CBT	Anxiety (STAI, state subscale)[a]	*Domar* et al. *(2015)*	89	43.48 (7.83)	40.6 (12.33)	42.91	37.78	−5.13	−12
		Kim et al. *(2014)*	26	40.96 (9.91)	28.12 (5.2)				
	Depression (BDI)[a]	*Faramarzi* et al. *(2008)*	29	20.1 (7.9)	7.7 (4.8)	16.51	9.83	−6.68	−40
		Gojani et al. (2018) (PRCI group)	35	18.55 (9.00)	13.14 (9.7)				
		Gojani et al. (2018) (PSS training group)	34	19.13 (8.67)	12.52 (8.05)				
		McNaughton-Cassill et al. *(2022)*	26	6.35 (6.96)	4.25 (5)				
	Quality of life (FertiQoL core score)[b,c]	*Domar* et al. *(2015)*	89	67.6 (14.02)	71.58 (14.23)	68.15	72.02	3.87	6
		Heredia et al. *(2020)*	11	72.59 (NR)	75.56 (NR)				
Mindfulness	Anxiety (STAI, state subscale)[a]	*Chan* et al. *(2012)*	141	44.79 (11.47)	41.58 (10.19)	45.64	41.98	−3.66	−8
		Galhardo et al. *(2013)*	55	47.82 (13.90)	43.02 (8.70)				
	Depression (BDI)[a]	*Galhardo* et al. *(2013)*	55	11.02 (7.05)	6.18 (4.05)	14.74	8.13	−6.60	−45
		Kalhori et al. *(2020)*	45	20.77 (6.35)	10.82 (7.16)				
		Nery et al. *(2019)*	62	13.66 (9.95)	7.92 (8.17)				
	Quality of life (FertiQoL core score)[b,c]	*Li* et al. *(2016)*	58	60.98 (NR)	73.89 (NR)	NA	NA	12.91	21

[a] A decrease in score from baseline or negative change in score indicates an improvement.

[b] An increase in score or positive change in score indicates an improvement.

[c] Core FertiQoL scores were calculated by summing the scores of the emotional, mind–body, relational and social subscales and dividing by 4.

BDI, Beck Depression Index; CBT, cognitive behavioural therapy; FertiQoL, Fertility Quality of Life tool; n, number of participants; NA, not applicable; NR, not reported; PRCI, positive reappraisal coping intervention; PROM, patient-reported outcome measure; PSS, problem-solving skills; STAI, State-Trait Anxiety Inventory.

DISCUSSION

The provision of psychosocial interventions could add value in fertility treatment. The purpose of this study was to present a proof-of-concept business case from a VBHC perspective for providing either CBT or a mindfulness intervention (via a website application) to women seeking fertility treatment, compared with no such psychosocial support. The primary studies reviewed suggested that CBT and mindfulness had the potential to lead to improvements in clinical outcomes and the cost-saving analysis suggested savings compared with women who did not receive such support. These findings may be helpful in conversations among fertility treatment stakeholders about implementing an integrated approach in practice. The pattern of findings could suggest that savings are a result of treatment persistence. Replication is needed owing to the small number of studies. In particular, the potential cost savings related to mindfulness warrants further re-evaluation as new data on its effect on clinical pregnancy rates becomes available. If the effect of mindfulness in the one available study was over- or underestimated, then so would our estimates.

A business case is only as good as its underlying data, and the low quality of existing evidence on this topic is a known issue (*Verkuijlen et al., 2016*). Nevertheless, the current business case can serve as a basis and be updated as data from higher quality studies become available. In practice, fertility clinics may use this business case as a framework for implementing psychosocial interventions as a pilot study and for evaluating its usefulness for all fertility treatment stakeholders in their context prospectively.

There are multiple reasons why psychosocial interventions may have benefits. As meta-analyses examining pre-treatment stress and IVF outcome generally show no association (*Boivin et al., 2011b*; *Nicoloro-SantaBarbara et al., 2018*; *Peaston et al., 2022*), it is more likely that interventions help people modify thoughts and behaviours that compromise fertility or affect quality of life. For example, CBT may help reduce catastrophising thoughts, thereby helping people persist with treatments that have favourable prognosis but which are psychologically demanding (*Cottle et al., 2018*). Furthermore, these meta-analyses conclude that a large

TABLE 3 PUBLISHED CLINICAL PREGNANCY AND FERTILITY TREATMENT DISCONTINUATION RATES COMPARING WOMEN WHO RECEIVED EITHER CBT OR TRAINING IN MINDFULNESS DURING FERTILITY TREATMENT WITH THOSE WHO DID NOT

Intervention	Outcome evaluated	Study (Year)	Rate, %		Sample size, *n*	
			Intervention group	Control group	Intervention group	Control group
CBT	Clinical pregnancy rate	*Domar* et al. *(2015)*	34.5	35.2	87	71
		Gorayeb et al. *(2012)*	39.8	23.2	93	95
		Haemmerli et al. *(2010)*	5.8	11.3	52	53
		Weighted mean	30.2	24.2	NA	NA
	Discontinuation rate of fertility treatment	*Domar* et al. *(2015)*	5.5	15.2	55	46
Mindfulness	Clinical pregnancy	*Li* et al. *(2016)*	44.8	26.0	58	50

CBT, cognitive behavioural therapy; NA, not applicable.

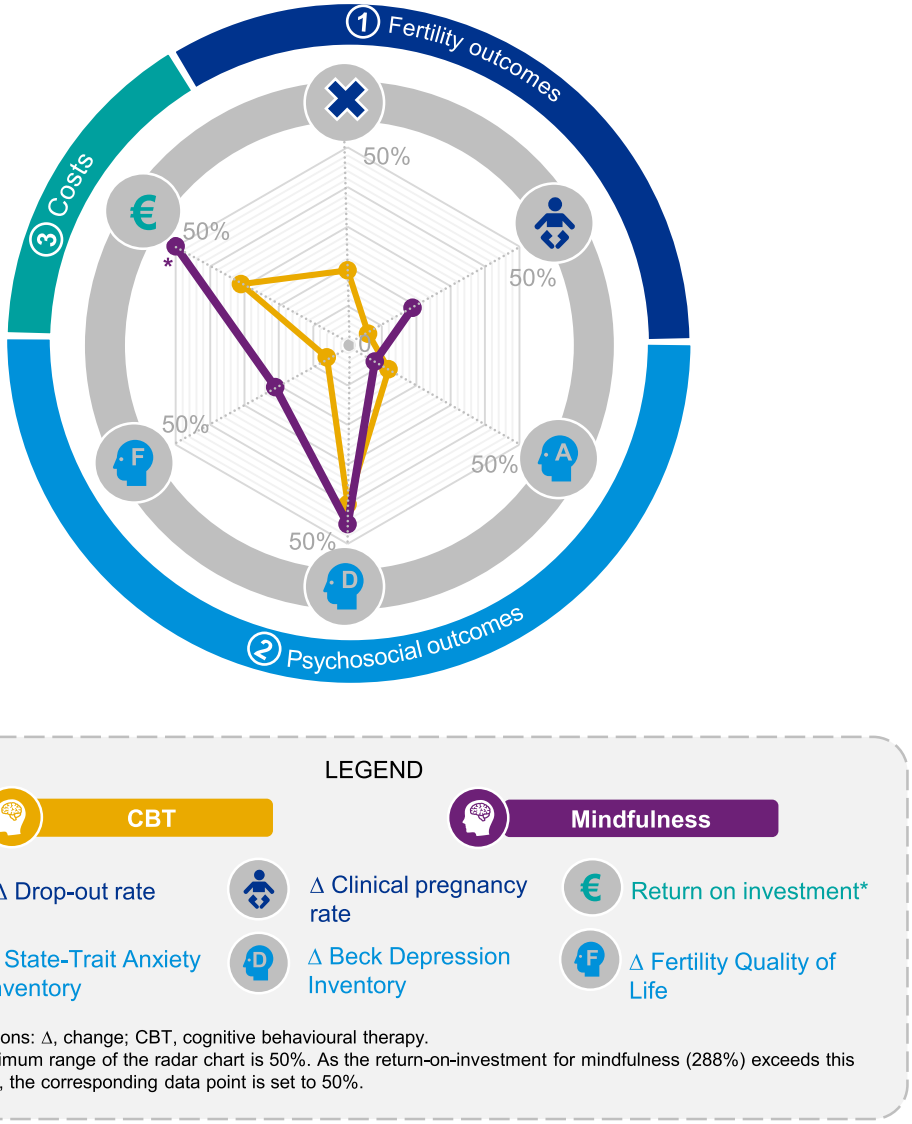
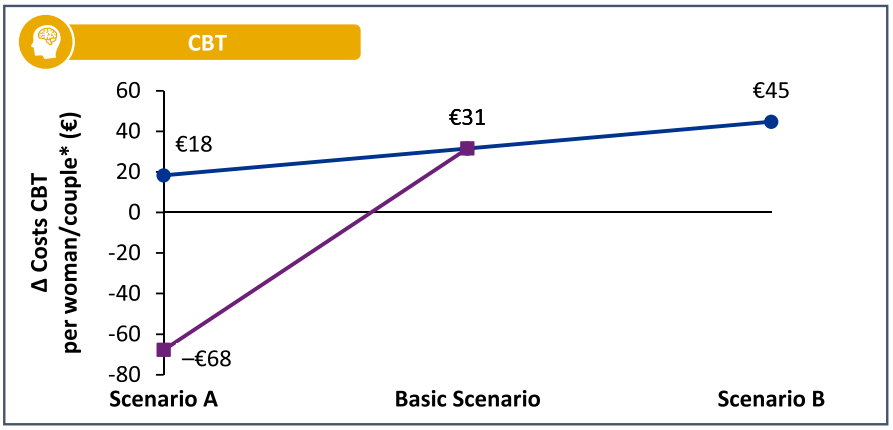
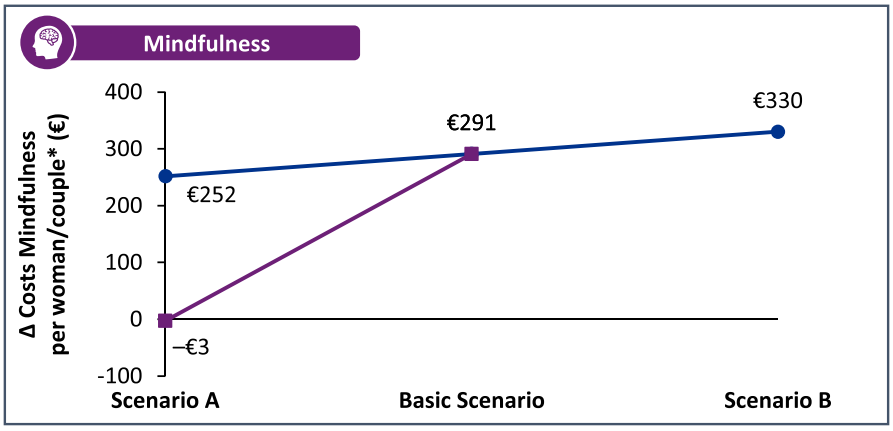
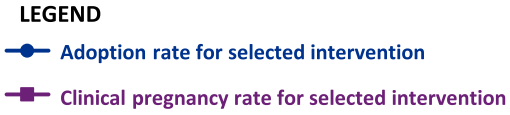


FIGURE 1 Value of providing cognitive behavioural therapy or mindfulness to women seeking fertility treatment compared with no psychosocial support in terms of fertility, psychosocial and cost outcomes. Values shown for fertility outcomes represent percentage point differences, values for psychosocial outcomes represent per cent change as (post-intervention score − pre-intervention score)/pre-intervention score, and values shown for costs represent return on investment (see Materials and methods). Note that no data point is available for the change in drop-out rate (from fertility treatment) for mindfulness, owing to a lack of empirical data.







Abbreviation: Δ, change

*In the Netherlands, costs for IVF/ICSI/IUI are approximately the same regardless of the patient's relationship status; that is, whether donor sperm or sperm from their partner is used.

FIGURE 2 Results of the sensitivity analysis showing the changes in potential cost savings per woman or couple depending on the adoption rate and the clinical pregnancy rate used. Adoption rate is defined as the percentage of couples and individuals willing to make use of the psychosocial intervention during treatment. For both CBT and mindfulness, the lower adoption rate used in scenario A, i.e. 25%, indicates less cost savings per woman or couple, whereas a higher rate used in scenario B, i.e. 31%, higher cost savings. With the clinical pregnancy rates, a lower clinical pregnancy rate (1% for CBT, 5% for mindfulness; scenario A) changes the potential cost savings per woman or couple to extra costs for both psychosocial interventions. The maximal value for the change in clinical pregnancy rate, i.e. the best possible case regarding achieved pregnancies due to intervention, was assumed to be equivalent to that in the basic scenario. Hence, there is no scenario B.

variability exists in these studies, which can make conclusions more challenging to reach.

The added value attributable to providing psychosocial support may be under- or overestimated; therefore, these findings need to be interpreted cautiously. First, this business case did not include the effect of providing psychosocial support on societal costs, such as work productivity. Average overall absence from work during IVF treatment has been reported to be 33 hours, and women with emotional distress report significantly more IVF-related absence from work (*Bouwmans et al., 2008*). Providing psychosocial support during fertility treatment may provide more value than estimated in our study by preventing lost productivity. Second, the potential effect of psychosocial support reducing rates of fertility treatment discontinuation was not included in the evaluation of costs. It is possible that if fewer women decide to discontinue fertility treatment, this may result in more treatment cycles, leading to higher fertility treatment costs in addition to an improvement in quality of care and quality of life for the patient and their partner. Third, the effect of providing CBT or mindfulness was evaluated in relation to the first ART cycle only. The effect on cumulative cycles is, therefore, unknown. Research indicates that the psychosocial effect of infertility extends to decades after stopping fertility treatment (*Gameiro et al., 2016*; *Payne et al., 2021*), suggesting that infertility-related anxiety and

depression may become chronic conditions that require long-term treatment. As such, the current business case may underestimate the value of psychosocial interventions. Fourth, the interventions were focused on the women, not the couple as a whole or the male partner, which may underestimate the added value of CBT, mindfulness, or both. *Dong et al. (2022)* recently reported that 'increased infertility duration is an independent risk factor for the occurrence of sexual dysfunction' in men. Future evaluations should include these four aspects and validate our findings with real world data. Finally, while the potential cost savings, particularly for CBT, diminish with the inclusion of individual counselling sessions or reverse into extra costs at lower clinical pregnancy rates, the potential extra costs are arguably worthwhile in view of improvements in depressive symptoms, anxiety and fertility quality of life. These outcomes relate to the VBHC concept of comfort ('relief from physical and emotional suffering') (*Teisberg et al., 2020*).

Limitations

One of the main limitations of this study was the small number of included studies. This was related to the heterogeneous nature of psychosocial interventions described in published research. A previous Cochrane review suggested against pooling different types of interventions (*Verkuijlen et al., 2016*); therefore, strict definitions were followed for the CBT and mindfulness interventions included during the study selection process. Also, not all studies included data on each outcome of interest. As such, the effect of CBT or mindfulness on psychosocial outcomes were based on data from one to three studies only. Data on fertility outcomes were particularly limited for mindfulness, with no data available for discontinuation of fertility treatment, and only one study providing data on clinical pregnancy rates. Moreover, the included studies had limited sample sizes, which can increase the risk of spurious findings. The difference in clinical pregnancy rate attributable to an intervention is a key driver of the estimated cost saving and corresponding ROI; therefore, the cost outcomes, especially that of mindfulness, must be interpreted with caution. For mindfulness, the sensitivity analysis showed that a 5% clinical pregnancy rate (which is close to the 6% used in the basic scenario for CBT) is associated with extra costs instead of cost savings. In addition, the potential cost savings and corresponding ROI may be influenced by the unit cost of the psychosocial intervention used in the cost model. Because of intervention heterogeneity and need to cost on a homogeneous format, a standard delivery format and unit cost based on the Mental Stark programme was assumed (self-administered, online, chat function with professional, optional two in-person sessions). The content is similar to that provided in the included studies and the digital format aligns with the sort of services offered in other health systems such as the NHS (*National Institute for Health and Care Excellence, 2024*). It is possible that the chosen delivery format may not be the ideal format to yield the gains reported in included studies. Also, the ROI will be proportionally lower if the unit costs (based on another delivery format) are higher and *vice versa*. Furthermore, the included studies had small sample sizes and were not evaluated for risk of bias.

The generalisability of the findings may be limited in two ways. First, data on the psychosocial and fertility outcomes came from international studies and may, therefore, not be completely representative for the Dutch situation. Second, the data on costs and proportions of women undergoing IUI, IVF or ICSI are based on Dutch data, which may not be representative of other countries. Nevertheless, our evaluation was informed by published scientific research, and calculations and assumptions were validated by experts in medical and health psychology, reproductive science, fertility, and gynaecology.

Future considerations

Future business cases should test other psychological approaches that were excluded in the current prototype. Furthermore, to optimise the benefits of psychosocial support, future research should investigate the reasons why some women (or couples) accept the offer for such support and others do not. One reason is a mismatch between the type of support offered and needs; therefore, psychosocial support needs to be tailored to the women or partner and treatment journey stage (*Boivin and Gameiro, 2015*; *Boivin et al., 2022*). Customised psychosocial support may be particularly valuable at critical decision-making moments, such as non-biological parenthood, whether to discontinue fertility treatment (*Abramov et al., 2022*), and for prevention of chronic infertility-related anxiety and depression (*Gameiro et al., 2016*; *Payne et al., 2021*). Recent findings suggest that the process of determining the need for, and customising psychosocial support, should be based on the following five categories of determinants of medical help-seeking behaviour for infertility: sociodemographic (age, gender, race and ethnicity, relationship status); socioeconomic (income, socioeconomic status, education level, health insurance); reproductive history (parity, miscarriages, endometriosis, uterine fibroids, polycystic ovarian syndrome); attitudes (attitudes about infertility and treatment, social pressure and support, stigma, religious beliefs, self-perception, intent for a child, importance of parenthood); and psychological factors (treatment anxiety, depressive symptoms, stress and coping, locus of control) (*Passet-Wittig and Greil, 2021*). An evaluation of attitudes, societal and political attitudes towards infertility and interventions regarding infertility shows that these factors may be particularly influential, as in the case of Israel, for example, where pregnancy is strongly encouraged (*Greil et al., 2011*).

In conclusion, the negative psychosocial consequences of an unfulfilled child wish and fertility treatment are considerable. Providing CBT or mindfulness to women seeking fertility treatment (before their first cycle of fertility treatment) has added value, and potential to lead to less anxiety and depressive symptoms, higher quality of life and pregnancy rate, lower discontinuation rates, and cost savings. Information from a business case based on the VBHC perspective may help decision makers determine rationally whether integrating psychosocial interventions as a standard component of fertility treatment is worthwhile.

DATA AVAILABILITY

Data will be made available on request.

ACKNOWLEDGEMENTS

This work was supported by Ferring BV. Funding was provided for fertility expert working group advisory board meetings, the cost-effectiveness modelling of the psychosocial support interventions and medical writing support. We would like to thank Dr JW Schoones, information

specialist (Directorate Research, Leiden University Medical Centre) for his assistance with the literature search and Kimi Uegaki, PhD (iWrite) for her assistance with preparing the manuscript.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.rbmo.2024.104113.

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Received 6 February 2024; received in revised form 7 May 2024; accepted 10 May 2024.