Women's health and wellbeing: the roles of early life adversity, stress and lifestyle

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Chapter 7

The long-term effects of a preconception lifestyle intervention in obese infertile women on perceived stress, mood symptoms, sleep and quality of life

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Background

Obesity is an increasing problem worldwide and is associated with serious health risks. Obesity does not only reduce physical health, but can also negatively affect levels of perceived stress, mood symptoms, sleep quality and quality of life (QoL), which may lead to further weight gain. We have previously shown that a preconception lifestyle intervention reduced weight and improved physical QoL in the short term. In the current study, we assessed the long-term effects of this intervention in obese infertile women on perceived stress, mood symptoms, sleep quality and QoL.

Methods and findings

We followed women who participated in the LIFEstyle study, a multi-center randomized controlled trial. Participants were 577 infertile women between 18 and 39 years of age with a body mass index (BMI) ≥ 29 kg/m^2. Participants in the intervention group received a six-month lifestyle intervention to improve diet and increase physical activity followed by infertility treatment. Women in the control group received prompt infertility treatment. Perceived stress, mood symptoms, sleep quality and QoL were measured five years after randomization. T-tests and linear regression models were used to assess differences between the intervention and control group.

Five years after randomization, no differences were observed for perceived stress, mood symptoms, sleep quality and QoL between the intervention (n=84) and control group (n=94). There was selective participation: women who did not participate in the follow-up had lower baseline mental QoL, and benefitted more from the intervention in terms of improved physical QoL during the lifestyle intervention.

Conclusions

Although a preconception lifestyle intervention improved physical quality of life on the short term, we found no evidence that these effects were maintained over time, possibly due to selective participation in the follow-up. Future work is needed on the long-term effects of lifestyle interventions on well-being.

Introduction

Obesity is an increasing health problem across the world, with rates as high as 40% among adults in the US (1). In Europe the prevalence of overweight in 2014 has been estimated to be almost 40%, and obesity 16% (2). Obesity does not only reduce physical health (3), but may also have adverse consequences for mental health and quality of life (QoL). Obesity was associated with lower self-reported QoL in adults, and this lower QoL was even more evident in those with increasing degrees of obesity (4). Weight gain in overweight women was associated with higher levels of psychological and perceived stress (5). Furthermore, depressive and anxiety disorders seem to be more prevalent in people with obesity, especially among women and those with severe obesity (6). A bidirectional pathway might explain the causal links between obesity and depression, in which obesity leads to more depressive symptoms, and depressive symptoms lead to physiological and psychosocial alterations associated with weight gain (7). Subclinical depression and impaired mental wellbeing were associated with excess mortality (8, 9). Obesity was also associated with short sleep duration and low sleep quality, which in turn was associated with weight gain (10). The higher prevalence of obstructive sleep apnea in obese adults is one of the possible causes of impaired sleep quality (10). Low sleep quality was associated with lower QoL, more depressive symptoms and an increased cardiovascular disease risk (11-13). This underlines the importance of intervening in the vicious circle of obesity and impaired mental wellbeing, in order to not only improve physical but also psychological outcomes.

Lifestyle interventions are the first step in the treatment of overweight and obesity. In women, the preconception period is a good time window to try to change lifestyle, since women are especially receptive to lifestyle advice in this period (14). In the LIFEstyle study, obese infertile women were randomized between a lifestyle intervention group and a control group. During and directly after the six-month intervention period women in the lifestyle intervention group weighed less, less often had metabolic syndrome and reported better physical QoL scores compared to the control group (15).

Lifestyle interventions aimed at weight loss have previously been shown to reduce the risks of associated mood problems and impaired sleep quality. A systematic review and meta-analysis showed that lifestyle interventions aiming at weight loss, reduced symptoms of depression as well (16). In addition, two behavioral weight loss interventions demonstrated better sleep quality after a successful reduction in body weight (17). However, these reductions were observed

during the intervention period, or immediately after the intervention. Long-term effects of lifestyle interventions on weight reduction are disappointing (18), and research regarding the effects of lifestyle interventions on long-term wellbeing and sleep quality is scarce. Such research is highly relevant as mental wellbeing and good sleep quality are important determinants of adequate daily life functioning, and could possibly increase motivation to lose weight and lead to better weight maintenance (19).

We investigated whether a preconception lifestyle intervention in obese infertile women leads to improved levels of perceived stress, mood symptoms, sleep quality and QoL in the long-term.

Methods

We followed women approximately five (range= 3-8) years after participation in a preconception lifestyle intervention trial (20), the LIFEstyle study (21, 22). The LIFEstyle study was a randomized controlled trial (RCT) carried out in 23 hospitals in the Netherlands between 2009-2012. Women were eligible for the LIFEstyle study if they had a body mass index (BMI) of ≥ 29 kg/m², were between 18 and 39 years of age and were infertile. Infertility was defined as chronic anovulation or if women had an ovulatory cycle and had unsuccessfully tried to conceive for at least 12 months. In total 577 obese infertile women were randomized between a six-month lifestyle intervention group, and a control group. The six-month lifestyle intervention aimed at 5-10% weight loss or a BMI < 29, through a healthy diet, increased physical activity and behavioral modification. Behavior change was targeted by motivational counselling aimed at the awareness of lifestyle behavior leading to obesity and providing information about healthy lifestyle effects on infertility and pregnancy chances and outcomes. Individual lifestyle goals were formulated and listed in a patient contract. Trained coaches guided the lifestyle intervention, which consisted of six outpatient visits and four telephone consultations during the six-month intervention period. The intervention group received infertility treatment as indicated after the six-month intervention period, or if the weight loss goal of the intervention was reached before the six-month period ended. The control group received prompt infertility treatment. The results of the effect of the lifestyle intervention on fertility and pregnancy outcomes have been published previously (22). Rates of a vaginal birth of a healthy singleton at 37 weeks or more, the primary outcome of the study, were not higher in the intervention group, compared to the control group (22). The lifestyle intervention significantly reduced weight and led to improved cardiometabolic health and physical QoL in the short-term (15).

The long-term follow-up of the LIFEstyle study involved 564 eligible women. Eligible women of whom contact information was known (n=550) received an information leaflet at home regarding the follow-up. The five year follow-up consisted of a questionnaire with items regarding QoL and symptoms of depression and anxiety. This questionnaire also included items regarding education level, self-reported weight, and if a woman gave birth to a child. All eligible women were also invited to participate in a separate visit involving physical measurements and an additional questionnaire in which perceived stress and sleep quality were measured. The primary focus of the physical measurements was to assess anthropometrics and cardiometabolic health. The median number of months between the basic questionnaire and additional visit/questionnaire was five months.

Baseline information at the time of randomization was available for age, ethnic background, education level, BMI, polycystic ovary syndrome (PCOS) diagnosis and if a woman ever conceived.

Perceived stress

The 10-item perceived stress scale (PSS) was used to measure perceived stress (23). This questionnaire has been labelled a valid and internally consistent measure of perceived stress (24). A total score was calculated as a sum score from the 10 items.

Mood symptoms

For the assessment of symptoms of depression and anxiety, the hospital anxiety and depression scale (HADS) was used (25). This 14-item questionnaire has demonstrated good sensitivity and specificity (26). Seven items measure symptoms of depression, and the other seven items measure symptoms of anxiety. The total score for depression and anxiety is the sum score of these items.

Sleep quality

The Pittsburgh sleep quality index (PSQI) was used to measure sleep quality. This questionnaire consists of 19 items, with seven subscales from which a total score can be derived, with higher scores indicating worse sleep quality (27). The subscales are 'subjective sleep quality', 'sleep duration', 'sleep disturbances', 'sleep latency', 'day dysfunction', 'habitual sleep efficiency', and 'use of sleeping medication'. The PSQI has shown good validity and internal consistency (27).

Quality of life

QoL was measured with the short form 36 (SF-36), a questionnaire with 36 questions regarding physical and mental QoL (28), and has demonstrated good validity (29). Higher scores indicate better QoL. The subscales 'physical functioning', 'role limitations physical problem', 'bodily pain', 'general health' and 'vitality' form the physical component summary (PCS) of the QoL. The subscales 'social functioning', 'role limitations emotional problem', 'mental health' and 'vitality' form the mental component summary (MCS) of the QoL. Baseline SF-36 data at time of randomization was also available.

Statistical analyses

Comparisons of follow-up characteristics for the intervention and control group were performed. Potential selection bias was assessed by comparing the baseline

characteristics between participants and non-participants in the follow-up. These assessments were performed with *t*-tests, Fisher-Freeman-Halton tests and chi-square tests. The comparisons between the intervention and control group for levels of perceived stress, symptoms of depression and anxiety and sleep quality were analyzed with *t*-tests. The change in the subscales and component scores of QoL was calculated and used as the outcome in univariate regression models, covarying for the baseline measurement of that outcome, and randomization group was used as factor. Results were considered statistically significant if a p value was < 0.05. Statistical analyses were performed using IBM SPSS version 24.0 (Armonk, NY, USA).

Results

Participants flow and characteristics

Figure 1 shows the flow of the 550 women invited to take part in the follow-up study. A total of 178 (32%) women participated in the follow-up of whom 84 women had been allocated to the intervention group and 94 women to the control group. They filled out the questionnaires regarding depression, anxiety and QoL. The additional questionnaire measuring perceived stress and sleep quality was filled out by 115 women (21%), 52 intervention women and 63 control women. In Table 1 the differences at baseline between the participants and non-participants in the follow-up are shown.

Non-participants in the follow-up were less often Caucasian, had less often PCOS, and had lower scores on the QoL subscales 'social functioning', 'role limitations – emotional problem' and 'mental health', indicating worse mental QoL. The mental component summary was also significantly lower at baseline for non-participants in the follow-up. The subscales 'social functioning' and 'mental health' were significantly better at baseline in the intervention group of participants, and the subscale 'role limitations – emotional problem' and the mental component summary were significantly better at baseline in both the intervention and control group of participants compared to non-participants in the follow-up. Furthermore, the improvement in physical QoL in the short-term in the intervention group was predominantly among women who did not participate in the follow-up ($p = 0.01$ for non-participants in the follow-up, $p = 0.16$ for follow-up participants). The participant characteristics at follow-up were similar between the intervention and control group, as shown in Table 2. Self-reported BMI at follow-up was similar for the intervention and control group.

Perceived stress, mood symptoms, sleep quality and quality of life

Table 3 and 4 show the results of the lifestyle intervention on long-term levels of perceived stress, mood symptoms, and sleep quality. No differences were observed between the intervention and control group for levels of perceived stress, symptoms of depression and anxiety, or sleep quality. In Table 5, the results for QoL also showed no difference in change from baseline to follow-up between the intervention and control group. No differences were observed between the intervention and control group for any of the outcomes when participants were divided into women with a child, and women who never conceived (data not shown).

Discussion

In this five year follow-up visit of a preconception lifestyle RCT in obese infertile women, we were unable to detect any effects on levels of perceived stress, symptoms of depression and anxiety, sleep quality and QoL among those who participated in the follow up.

There are several potential explanations for the null findings in our study. First, a preconception lifestyle intervention might not lead to improved levels of perceived stress, mood symptoms, sleep quality and QoL in the long-term. On the other hand, the effects of the lifestyle intervention on long-term well-being and sleep quality might only be present if weight loss is maintained over time. Furthermore, this study was not powered for studying effects on long-term mental health. Relatively small differences cannot be detected with the current sample size (post-hoc power QoL: 33%). If all eligible women would have participated in the follow-up we would have had 80% power, and the currently observed difference in QoL between the intervention and control group would have been statistically significant.

Only 32% of the women who were invited to participate, filled out the questionnaire, and an even smaller group filled out the additional questionnaire (21%). Mental QoL at baseline was lower among women who did not participate in the follow-up, indicating that women with lower mental wellbeing were less interested in participation or less able to participate in follow-up measurements, possibly because they were less motivated. This baseline difference in mental QoL was more pronounced in the intervention group, which might have led to an underestimation of the long-term effect of the lifestyle intervention on mental QoL. Moreover, the short-term positive effect of the lifestyle intervention on physical QoL was predominantly among women who did not participate in the follow-up, and not among women who did participate in the follow-up. This indicates that a specific subgroup of women participated in the follow-up, predominantly those women who did not benefit from the intervention in terms of improved physical QoL during the lifestyle intervention. If all women who participated in the original trial had also participated in the follow-up study, we might have detected positive effects of the intervention on mental well-being and sleep quality.

Our null findings are not in line with a previous study examining long-term effects of a lifestyle intervention. In the Look AHEAD trial, a lifestyle intervention in overweight and obese individuals with type 2 diabetes led to improved mood in the short and long-term, which was eight years in that study (30). The lifestyle intervention also led to long-term maintained weight loss (31), which was not the case

in the selective group that participated in our follow-up, and could partially explain our findings. Besides weight and mood symptoms, QoL was also assessed in the Look AHEAD trial, and over time a reduction was observed in physical and mental QoL, with a smaller reduction in the intervention group, compared to the control group (30). QoL also reduced over time in the participants of our study, but this decline was not significantly different between the intervention and control group. The minimal clinically important difference for QoL measured by the SF-36 has been estimated to be 2-4 points, while in our results a difference in decline between the intervention and control group was approximately 1.5 point for physical QoL and 0.3 point for mental QoL. Hence, even with sufficient power, the long-term differences in QoL between the intervention and control group would not have been clinically relevant. The reduction of QoL over time has been documented in previous research, also among women in the same age group as our sample. This reduction has been associated with increasing age, suggesting a relation with an increased prevalence of disease over time (32, 33).

A strength of this study is the assessment of QoL at baseline and follow-up, providing information about changes in QoL over time. Limitations include selective participation and the lack of baseline and short-term data for perceived stress, mood symptoms and sleep quality. As a result we do not know if the intervention had any short-term effects on these outcomes.

Despite promising short-term effects on body weight and QoL, we were unable to detect effects of a lifestyle intervention on levels of perceived stress, mood symptoms, sleep quality and Qol in obese infertile women five years after randomization. However, future research regarding lifestyle intervention should investigate long-term effects on these outcomes, since mental wellbeing and good sleep quality are determinants of daily functioning, and may lead to improved cardiometabolic health. In future research regarding lifestyle interventions, high attrition rates should be anticipated in power calculations, consequently increasing the number of initial participants. Furthermore, since selective participation leads to difficulties in the evaluation of the effectiveness and the generalizability of the results, novel strategies are needed to engage study subjects to participate in follow-up measurements.

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The authors report no conflicts of interest.

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Figure 1. Flowchart of participants LIFEstyle study.

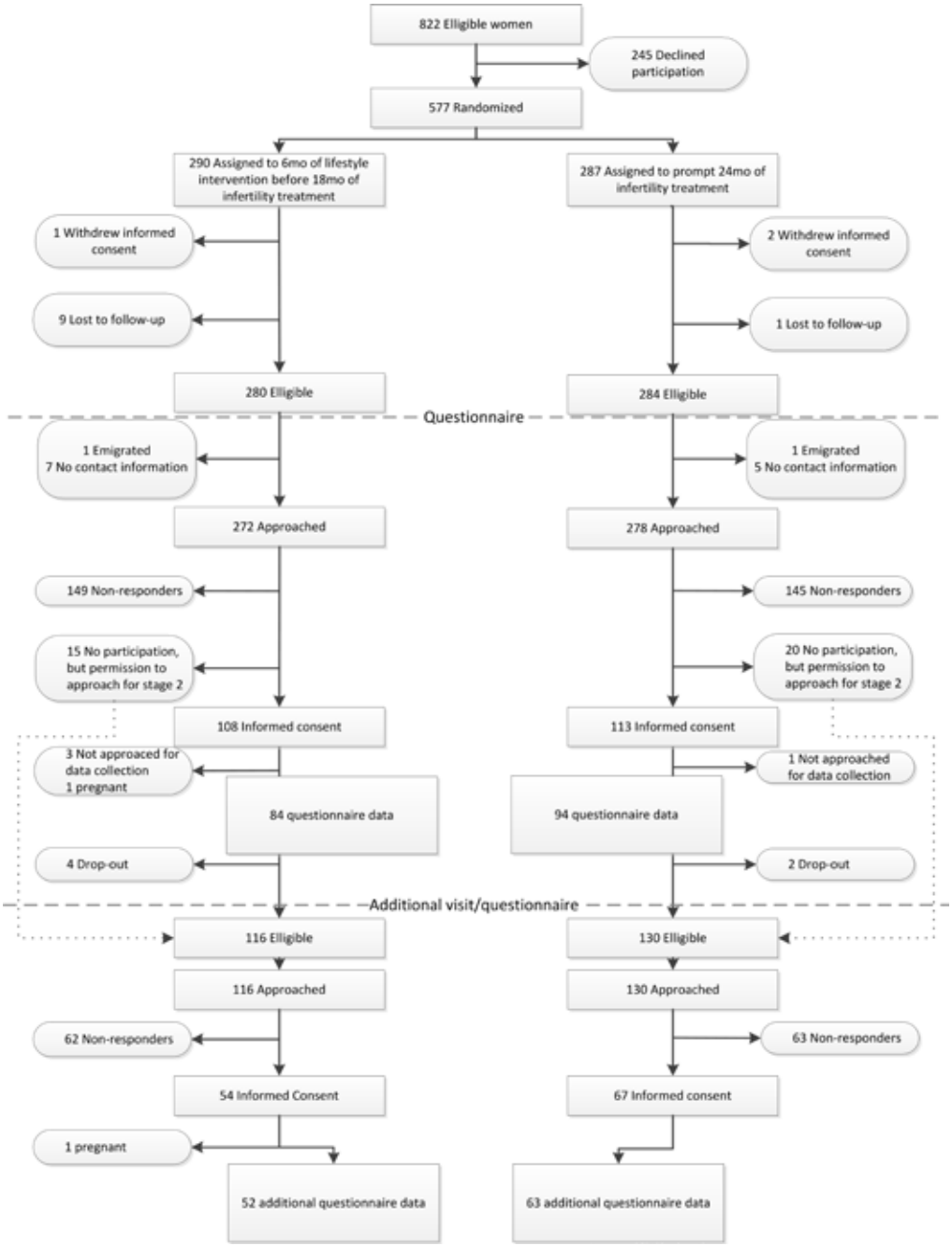

Table 1. Comparison of baseline characteristics of participants and non-participants in the follow-up of the LIFEstyle study.

	Participants (n=178)	**Non-participants in the follow-up (n=396)**	***p* value**
Age (mean, SD)	30.0 (4.2)	29.7 (4.7)	0.41
Caucasian (n, %)	169 (94.9)	333 (84.1)	< 0.01
Education level (n, %)			
Primary school Secondary education Intermediate vocational education Higher vocational education and university	5 (2.9) 33 (19.0) 96 (55.5) 39 (22.5)	22 (5.9) 98 (26.1) 170 (45.2) 86 (22.9)	0.07
Body mass index in kg/m^2 (mean, SD)	36.0 (3.2)	36.1 (3.5)	0.62
Polycystic ovary syndrome (n, %)	74 (41.6)	127 (32.2)	0.03
Never conceived (n, %)	114 (64.0)	255 (64.6)	0.91
Baseline quality of life (QoL) measures			
Physical functioning (mean, SD)	84.3 (15.5)	83.8 (17.4)	0.76
Role limitations – physical problem (mean, SD)	80.9 (36.6)	83.7 (32.6)	0.40
Bodily pain (mean, SD)	82.4 (22.8)	81.8 (23.7)	0.82
General health (mean, SD)	66.3 (17.5)	63.4 (18.4)	0.10
Vitality (mean, SD)	61.0 (16.0)	58.1 (17.4)	0.08
Social functioning (mean, SD)	86.4 (15.9)	81.3 (21.6)	< 0.01
Role limitations – emotional problem (mean, SD)	90.0 (25.4)	80.7 (34.9)	< 0.01
Mental health (mean, SD)	77.5 (12.2)	72.6 (16.0)	< 0.01
Physical Component Summary (PCS) (mean, SD)	49.3 (9.0)	50.2 (9.3)	0.36
Mental Component Summary (MCS) (mean, SD)	52.1 (7.4)	48.5 (10.5)	< 0.01

Table 2. Participant characteristics at follow-up.

	Lifestyle intervention group (n=84)	**Control group (n=94)**	***p* value**
Age (mean, SD)	35.1 (4.2)	34.8 (4.5)	0.64
Caucasian * (n, %)	78 (92.9)	91 (96.8)	0.23
Education level (n, %)			
No education	1 (1.2)	0 (0)	0.09
Primary school	0 (0)	4 (4.3)	
Secondary education	21 (25.0)	14 (14.9)	
Intermediate vocational education	41 (48.8)	53 (56.4)	
Higher vocational education and university	21 (25.0)	23 (24.5)	
Self-reported body mass index in kg/m^2 (mean, SD)	34.4 (5.1)	34.5 (5.0)	0.83
Polycystic ovary syndrome *, diagnosed by Rotterdam 2003 criteria (n, %)	32 (38.1)	42 (44.7)	0.37
No child (n, %)	18 (21.4)	15 (16.0)	0.35

* Measured at baseline.

Table 3. Symptoms of depression and anxiety measured by the HADS and perceived stress measured by the PSS five years after lifestyle intervention according to allocation status.

	Intervention group	**n**	**Control group**	**n**	**Mean difference (95% CI)**	***p* value**
Symptoms of depression	7.71 (0.41)	84	7.69 (0.33)	94	0.023 (-1.00 to 1.04)	0.97
Symptoms of anxiety	8.01 (0.42)	84	8.23 (0.34)	94	-0.22 (-1.28 to 0.84)	0.68
Perceived stress levels	14.38 (0.91)	52	13.73 (0.62)	63	0.65 (-1.47 to 2.78)	0.54

Data are given as means (SE); the mean difference between intervention and control group was assessed with student t-tests.

Table 4. Sleep quality measured by the PSQI, five years after lifestyle intervention according to allocation status.

	Intervention group (n=52)	Control group (n=63)	Mean difference (95% CI)	*p* value
Sleep quality total score	5.40 (0.50)	5.29 (0.43)	0.12 (-1.18 to 1.41)	0.86
- Subjective sleep quality	1.04 (0.11)	1.05 (0.09)	-0.01 (-0.29 to 0.27)	0.94
- Sleep duration	0.42 (0.10)	0.48 (0.10)	-0.06 (-0.35 to 0.24)	0.71
- Sleep disturbances	1.15 (0.07)	1.16 (0.06)	-0.01 (-0.19 to 0.18)	0.96
- Sleep latency	1.08 (0.14)	1.05 (0.13)	0.03 (-0.36 to 0.42)	0.88
- Day dysfunction	0.75 (0.09)	0.73 (0.09)	0.02 (-0.24 to 0.28)	0.88
- Habitual sleep efficiency	0.77 (0.14)	0.80 (0.13)	-0.03 (-0.41 to 0.35)	0.87
- Use of sleeping medication	0.13 (0.07)	0.18 (0.09)	-0.04 (-0.27 to 0.18)	0.71

Data are given as means (SE); the mean difference between intervention and control group was assessed with student t-tests.

Table 5. Quality of life measured by the SF-36, change from baseline scores five years after lifestyle intervention according to allocation status.

	Intervention group (n=65)	Control group (n=84)	Mean difference (95% CI)	*p* value
Physical functioning	0.70 (2.03)	-1.00 (1.84)	1.70 (-3.74 to 7.14)	0.54
Role limitations – physical problem	-1.80 (4.14)	-8.36 (3.72)	6.56 (-4.45 to 17.57)	0.24
Bodily pain	-5.95 (3.00)	-10.09 (2.70)	4.14 (-3.86 to 12.14)	0.31
General health	-17.56 (0.44)	-17.78 (0.39)	-0.22 (-0.94 to 1.38)	0.71
Vitality	-1.83 (2.29)	-7.25 (2.07)	-5.43 (-0.67 to 11.52)	0.08
Social functioning	-3.29 (2.41)	-4.29 (2.18)	1.01 (-5.43 to 7.44)	0.76
Role limitations – emotional problem	-6.40 (3.91)	-6.72 (3.51)	0.32 (-10.09 to 10.72)	0.95
Mental health	-2.95 (1.68)	-2.39 (1.52)	-0.56 (-5.07 to 3.95)	0.81
Physical Component Summary (PCS)	-2.45 (1.03)	-3.91 (0.91)	1.46 (-1.26 to 4.17)	0.29
Mental Component Summary (MCS)	-1.59 (1.09)	-1.90 (0.96)	0.31 (-2.56 to 3.18)	0.83

Data are given as mean change scores (SE), adjusted for baseline measurement; the mean difference between intervention and control group was assessed in univariate regression models.