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Effects of supervised exercise training during pregnancy on psychological well-being among overweight and obese women. Secondary analyses of the ETIP-trial, a randomized controlled trial.

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Abstract

Objectives: Overweight and obese women have increased risk for symptoms of anxiety and depression during pregnancy and postpartum. In this pre-specified secondary analysis from the Exercise Training in Pregnancy (ETIP) trial, our aim was to examine effects of supervised exercise during pregnancy on psychological well-being in late pregnancy and postpartum among women with a pre-pregnancy body mass index (BMI) ≥ 28 kg/m^2.

Design: Single-centre, parallel group, randomized controlled trial.

Setting: University Hospital, Norway

Participants: Ninety-one women (age 31.2±4.1 years, BMI 34.5±4.2 kg/m^2) were included and 72 and 70 completed data collection in late pregnancy and postpartum, respectively.

Intervention: The exercise group was offered three weekly supervised exercise sessions (35 minutes of moderate intensity walking/running, followed by 25 minutes of resistance training), from inclusion and until delivery.

Primary and secondary outcomes measures: Our primary analyses were based on intention to treat, with secondary per-protocol analyses. To assess psychological well-being, we used the «Psychological General Well-Being Index» (PGWBI) at inclusion (gestational week 12-18), late pregnancy (gestational week 34-37), and three months postpartum. Postpartum, we assessed depression using the «Edinburgh Postnatal Depression Scale» (EDPS).

Results: Baseline PGWBI for all women was 76.4±12.6. There was no difference between groups in PGWBI in late pregnancy; exercise 76.6 (95% CI 72.2, 81.0), control 74.0 (95% CI 69.4, 78.5) ($p = 0.42$). PGWBI increased postpartum; exercise 85.4 (95% CI 81.9, 88.8), control 84.6 (95% CI 80.8, 88.4) (with no between-group difference, $p = 0.77$). There was no between-group difference in EDPS; exercise 2.96 (95% CI 1.7, 4.2), control 3.48 (95% CI 2.3, 4.7) ($p = 0.55$).

Conclusions: We found no effect of supervised exercise training during pregnancy on psychological well-being in late pregnancy or postpartum, nor on the risk for postnatal

depression. The study participants reported good psychological well-being and had a low risk for postnatal depression.

Trial registration number: ClinicalTrials.gov NCT01243554

Key words: Maternal health, mental health, depression, anxiety, pregnancy complications

Article summary

Strengths and limitations of this study:

- Randomized controlled trial
- Supervised exercise program
- Multiple time points for assessments of psychological well-being; in early pregnancy, late pregnancy and three months postpartum
- Limited number of participants
- Low adherence to the exercise intervention

Introduction

About 20% of pregnant women report of reduced psychological well-being and symptoms of depression and anxiety during pregnancy and postpartum.[1-3] The prevalence of mental disorders is especially high among overweight and obese pregnant women.[1,2,4-8] This adds to the well documented increased risk for several other maternal and foetal complications in this population, such as gestational diabetes, maternal hypertension, pre-eclampsia and infants born large for gestational age.[9-14] Psychological well-being can be defined as "people's cognitive and affective evaluations of their lives; happiness, absence of negative emotions (e.g. depression, anxiety), satisfaction with life, and positive functioning".[15] Postnatal depression can be defined as "a type of clinical depression that occurs after childbirth".[16] Reduced psychological well-being may develop early in pregnancy, and symptoms of anxiety and depression in pregnancy or postpartum are associated with increased risk for complications e.g. hypertension, preterm birth, infant small for gestational age, lower rates of breastfeeding and impaired mother-newborn interaction.[17-21] Therefore, it is important to find strategies to prevent poor psychological well-being during pregnancy and the postpartum period.

Regular physical activity and supervised exercise training are beneficial for psychological well-being,[22-24] and contribute to reduced depressive symptoms among previously inactive individuals.[24] Pregnant women are advised to exercise and be physically active[25], but the frequency and intensity of exercise and physical activity tend to decline during pregnancy, especially among overweight and obese women.[26] Observational studies have found maternal exercise and physical activity to associate with better psychological well-being and reduced risk for postnatal depression.[27,28] However, results from randomized controlled trials (RCTs) on the effect of exercise training on psychological well-being diverge.[29-31]

In the Exercise Training in Pregnancy (ETIP) trial, we determined the effect of offering supervised exercise training during pregnancy on maternal and foetal outcomes among 91

overweight/obese women, with gestational weight gain as the primary outcome.[32-35] In this pre-specified secondary analysis of the ETIP trial, we aimed to determine the effect of exercise training on self-perceived psychological well-being in late pregnancy and three months postpartum, and the effect of exercise training in pregnancy on the risk for postnatal depression.

Methods

Trial design

The ETIP trial was a single-centre, parallel-group RCT where we determined the effects of offering overweight and obese women supervised exercise training during pregnancy compared to standard maternal care only. The trial was undertaken at the Norwegian University of Science and Technology (NTNU) and St. Olavs hospital, Trondheim University Hospital, Norway. We started inclusion in September 2010, with the last assessments in November 2015. The ETIP trial protocol and detailed description of the methods have been published elsewhere.[32,35] The study was approved by the Regional Committee for Medical and Health Research Ethics (REK-midt 2010/1522) and registered in ClinicalTrials.gov (NCT01243554).

Participants

We included women with pre-pregnancy body mass index (BMI) $\geq$ 28 kg/m^2, $\geq$ 18 year, in gestational week 12-18, carrying a singleton live foetus at an 11–14 week ultrasound scan. Participants had to attend assessments and exercise classes at St. Olavs hospital. We excluded women with high risk of preterm birth, diseases that could interfere with participation, or if they exercised twice or more weekly in the period before inclusion. The women received written information and signed informed consent on behalf of themselves and their offspring before inclusion into the trial. We recruited participants through invitations sent along with notices for routine ultrasound scan appointments, information sent to general practitioners, and through

Google advertisements. At the last study visit, the women received infant food worth 500 Norwegian kroner.

Intervention

All participants, regardless of group allocation, received maternity and postpartum care according to the Norwegian Standard Maternity Care for pregnant women, which is offered to all (free of charge).[36]

Women in the exercise group were offered supervised exercise sessions at St. Olavs hospital three times weekly from inclusion until delivery. The exercise program provided was in accordance with the recommendations from the American College of Obstetricians and Gynaecologists[25,37,38] and from the Norwegian Directorate of Health for physical activity during pregnancy.[39] The exercise sessions were supervised by a physical therapist and consisted of 35 minutes of treadmill walking at approximately 80% of maximal aerobic capacity (corresponding to Borg scale 12–15)[35] followed by 25 minutes of resistance training, including pelvic floor muscle training. In addition to the supervised program, we asked the women to exercise at home for 50 minutes twice weekly and to do daily pelvic floor muscle exercises. For a full description of the exercise intervention, see previous reports.[32,35] Adherence to the exercise program was registered in a training diary. Women in the control group were not discouraged from physical activity or exercise.

Outcomes

Self-perceived psychological well-being was assessed by the "Psychological General Well-Being Index" (PGWBI) questionnaire[40] at baseline (gestational week 12-18), in late pregnancy (gestational week 34-37) and three months postpartum. Postpartum the participants also completed the "Edinburgh Postnatal Depression Scale" (EPDS) questionnaire.[41] The women completed the questionnaires at the hospital while they underwent a 2 h oral glucose tolerance test, with trial researchers available to clarify questions if needed.

The PGWBI questionnaire contains 22 questions regarding self-perceived psychological health and general well-being, with both positive and negative affective states. The questions are grouped into six intrapersonal states (subscales); "Anxiety", "Depressed Mood", "Positive well-being", "Self-control", "General health", and "Vitality".[40] Each question has six response alternatives where value 0 is given for the most negative option, and value 5 for the most positive option. Depending of number of questions included, the range score in each subscale is from 0 to 15, 20 or 25. The PGWBI global score ranges from 0 to 110, with higher scores representing better psychological well-being.

The EPDS contains 10 questions assessing how the woman is coping with life changes related to pregnancy and childbirth. All questions contain four response alternatives. We estimated total score with use of a scoring system 1-4, with "1" representing the most negative option, and "4" the most positive option. A total score of <8 = "Depression not likely", 9-11 = "Depression possible", 12-13 = "Fairly high possibility of depression", ≥14 = "Probable depression". In addition, if the participant scored 1, 2 or 3 on question number 10, she was classified as "Suicidal risk".[41]

Additionally, the participants reported their perceived health status at baseline and in late pregnancy as either "very good", "good", "either good or bad", "quite bad" or "bad".

Sample size

The sample size calculation for the ETIP trial was based on difference between groups in the primary outcome (gestational weight gain) and is detailed elsewhere.[32,35] We have not performed a separate power calculation for the secondary analyses reported in this paper.

Randomization and blinding

Randomisation was performed before baseline assessments using a computer random number generator, developed and administrated at the Unit for Applied Clinical Research, NTNU. The personnel who provided the participants with questionnaires regarding psychological well-

being in late pregnancy and postpartum were not blinded for group allocation. Further details about randomization and blinding in the ETIP trial are published previously.[32]

Statistical methods

We confirmed baseline data normality using Shapiro-Wilk tests and visual inspection of plots and histograms. Comparisons between groups at baseline was analysed by independent samples t-tests and Fisher's Exact tests/Pearson Chi Square tests. We analysed between-groups differences in the effect of exercise training on psychological well-being (assessed by PGWBI) in late pregnancy and postpartum by general linear model analysis of covariance. Changes within-groups from baseline to late pregnancy and from late pregnancy to postpartum were also analysed by general linear model analysis of covariance. Baseline values were set as a covariate at late pregnancy analyses, and late pregnancy values were set as covariates at postpartum analyses. We analysed differences between groups in EDPS using an independent samples t-test. We assessed differences in baseline PGWBI between the participants who exercised per protocol and the non-adherent participants in the exercise group by independent samples t-tests. Due to the randomisation model, we assumed no systematic differences between groups at baseline. We based our primary analyses on the principle "intention to treat" and additionally performed "per protocol" analyses, according to pre-specified cut-off values for adherence to the exercise program.[35] No adjustment for multiple testing have been undertaken.

We used IBM SPSS Statistics 23. We consider P-values < 0.05 as statistically significant.

Results

We assessed 136 women for eligibility and included 91 women, with 46 in the exercise group and 45 in the control group. A detailed ETIP trial flow-chart is published elsewhere.[34] The number of participants analysed in late pregnancy was 74, and at three months postpartum 70. The exercise group exercised 31.7 ± 15.3 (range 0-53) sessions at the hospital and 19.2 ± 16.5 (range 0-72) sessions at home, giving a weekly average of 1.30 ± 0.8 supervised sessions and 0.8 ± 0.7 home-based sessions. About 50% (n=19) of the women in the exercise group exercised according to our pre-specified cut-off values for per protocol analyses.

Table 1 shows the baseline characteristics of the participants. There were no statistically significant differences between the groups at baseline. Full trial baseline data have been published previously.[32] At inclusion, 55% in the exercise group and 53% in the control group reported to fulfil the recommendations for physical activity (≥ 150 min/week of moderate intensity physical activity).

In late pregnancy, 61% in the exercise group and 66% in the control group reported to adhere to the recommendations for physical activity, with corresponding numbers postpartum being 72% in the exercise group and 79% in the control group. In late pregnancy, 77% in the exercise group compared to 23% in the control group ($p < 0.01$) reported regular exercise, with corresponding numbers postpartum being 46% in the exercise group and 25% in the control group ($p = 0.16$). About 58% in exercise group and 44% in the control group (between-group difference, $p = 0.35$) gained more weight during pregnancy than recommended by the Institute of Medicine.[42]

Table 1. Subjects characteristics at baseline for the exercise and the control group. Observed data are presented as means ± standard deviations, or number of participants with percentages. Psychological well-being is presented with the Psychological General Well-Being Index (PGWBI) global score and six subscales.

Subjects characteristics	**Exercise Group (*n* = 46)**	**Control Group (*n* = 45)**
	Mean ± SD/N (%)	*Mean ± SD/N (%)*
Age (years)	31.3 ± 3.8	31.4 ± 4.7
Body weight (kg)	95.3 ± 12.8	98.3 ± 14.2
Body mass index (kg/m²)	33.9 ± 3.8	35.1 ± 4.6
Weight classification		
Overweight, BMI 28.0–29.9 kg/m²	3 (6.6)	5 (11.1)
Class 1 obesity, BMI 30.0–34.9 kg/m²	28 (62.2)	19 (42.2)
Class 2 obesity, BMI 35.0–39.9 kg/m²	11 (24.4)	15 (33.3)
Class 3 obesity, BMI ≥ 40.0 kg/m²	3 (6.6)	6 (13.3)
Parity		
0	22 (47.8)	19 (42.2)
1	19 (41.3)	19 (42.2)
2	5 (10.9)	4 (8.9)
≥3	0 (0.0)	3 (6.7)
Current smoking	2 (4.7)	4 (8.9)
Education		
Primary/secondary school	1 (2.3)	3 (7.0)
High school	15 (34.1)	12 (27.9)
University ≤4 years	14 (31.8)	11 (25.6)
University >4 years	14 (31.8)	17 (39.5)
Currently employed	38 (82.6)	33 (73.3)
Self-perceived general health status		
Very good	0 (0.0)	4 (9.3)
Good	25 (54.3)	19 (49.4)
Either good or bad	18 (39.1)	20 (46.5)
Quite bad	3 (6.5)	0 (0.0)
Bad	0 (0.0)	0 (0.0)
Psychological General Well-Being Index (PGWBI)	76.6±11.1	76.2±14.3
Anxiety	19.8±3.3	19.2±4.6
Depressed mood	13.2±1.9	13.2±1.9
Positive well-being	12.2±2.8	12.6±3.1
Self-Control	12.9±1.7	12.0±2.5
General Health	9.7±2.8	9.5±2.7
Vitality	8.8±3.8	10.1±3.4
Missing: Education: Control: 1. General health status: Control: 3. PGWBI: Exercise; 2, control; 4. *Statistics:* Continuous variables were analysed by Independent samples t-test, "Current Smoking" and "Currently employed" were analysed by Fisher's Exact Test. "Weight classification", "Parity" and "Education" were analysed by Pearson Chi-Square Test.		

Psychological well-being in late pregnancy

We did not find any statistically significant difference between the groups in PGWBI global score, or in any of the six subscales, in late pregnancy (Table 2). The late pregnancy per-protocol analyses showed PGWBI global score of 80.2 (95% CI 73.9, 86.6) in the exercise group, and 74.7 (95% CI 70.4, 79.0) in the control group ($p = 0.15$) (Supplementary Table 1). No statistically significant difference between the exercise per-protocol group and the control group were found, but we observed a tendency of higher "Anxiety" score in the per-protocol exercise group (21.4) compared to the control group (19.5) ($p = 0.07$) (Supplementary Table 1). Figure 1 illustrates the changes in PGWBI global score and subscales from baseline to late pregnancy in each group.

Self-perceived general health status in late pregnancy was reported to be "Very good" by 9% in the exercise group and 11% in the control group, "Good" by 53% in the exercise group and 29% in the control group, "Either good or bad" by 21% in the exercise group and 50%, "Quite bad" by 15% in the exercise group and 11% in the control group, and "Bad" by 3% in the exercise group and none in the control group (between-group difference, $p = 0.37$). Results were similar in the per-protocol analyses.

Psychological well-being three months postpartum

We did not find any statistically significant difference between the groups in PGWBI global score, or in any of the six subscales three months postpartum (Table 2). The postpartum per-protocol analyses showed PGWBI global score of 84.8 (95% CI 79.5, 90.2) in the exercise group, and 85.3 (95% CI 81.5, 89.2) in the control group ($p = 0.88$), with no statistically significant differences in any of the six subscales (Supplementary Table 1). Figure 2 illustrates the changes in PGWBI global score and subscales from late pregnancy to postpartum in each group.

Table 2. Psychological general well-being (PGWBI), global score and subscales, in late pregnancy and three months postpartum. "Intention to treat" model based analyses with comparisons between groups presented as estimated mean difference with 95% confidence intervals (CI) and *p*-values.

	All participants	**Exercise**		**Control**		**Difference between groups**					
						Late pregnancy			**Postpartum**		
	Score at baseline N = 91	*Score late pregnancy N = 38*	*Score postpartum N = 36*	*Score late pregnancy N = 36*	*Score postpartum N = 34*	*Diff*	*95% CI*	*P-value*	*Diff*	*95% CI*	*P-value*
PGWBI	77.2	76.6 (72.2, 81.0)	85.4 (81.9, 88.8)	74.0 (69.4, 78.5)	84.6 (80.8, 88.4)	2.60	-3.77, 8.97	0.42	0. 77	-4.42, 5.95	0.77
Anxiety	19.7	20.7 (19.5, 22.0)	20.6 (19.5, 21.7)	19.6 (18.4, 20.8)	21.8 (20.7, 23.0)	1.12	-0.61, 2.86	0.20	-1.26	-2.98, 0.37	0.13
Depressed mood	13.4	13.2 (12.5, 13.8)	13.7 (13.2, 14.1)	13.1 (12.5, 13.8)	13.4 (12.9, 13.9)	-0.03	-0.88, 0.94	0.95	0.25	-0.43, 0.93	0.47
Positive well-being	12.5	12.0 (11.0, 13.0)	13.9 (13.0, 14.9)	12.5 (11.5, 13.5)	13.6 (12.7, 14.6)	-0.49	-1.93, 0.95	0.50	0.27	-1.07, 1.61	0.68
Self-Control	12.5	12.6 (11.7, 13.5)	13.6 (13.0, 14.1)	12.2 (11.3, 13.1)	13.1 (12.5, 13.7)	0.40	-0.87, 1.67	0.53	0.44	-0.38, 1.25	0.29
General Health	9.7	8.1 (7.1, 9.0)	11.5 (10.8, 12.2)	8.0 (7.0, 8.9)	11.2 (10.5, 11.9)	0.12	-1.24, 1.49	0.86	0.31	-0.72, 1.33	0.55
Vitality	9.5	9.8 (8.6, 11.0)	12.4 (11.3, 13.4)	9.2 (7.9, 10.4)	12.0 (10.9, 13.1)	0.65	-1.15, 2.44	0.47	0.38	-1.18, 1.94	0.63

Missing late pregnancy: Exercise 8, control, 5. *Missing postpartum:* Exercise 7, control 4.
Statistics: General linear model analysis of covariance with baseline mean and late pregnancy mean as covariates.
PGWBI = The Psychological General Well-Being Index (global score of all subscales).

Postnatal depression

We found no statistically significant difference in postnatal depression three months postpartum between the exercise (2.96, 95% CI 1.7, 4.2) and control group (3.48, 95% CI 2.3, 4.7) (p = 0.55). About 90% of the women in both groups reported a total score < 8, representing "Depression not likely". One woman in the exercise group and two in the control group reported a total score of 9-11; "Depression possible", and one women in each group reported a total score of 12-13; "Fairly high possibility of depression". One woman in the control group reported a score indicating suicidal risk. When analysing per-protocol, no statistical significant difference in total EPDS score was found between the exercise group (2.38, 95% CI 1.72, 4.2) and the control group (3.48, 95% CI 2.3, 4.7) (p = 0.30).

Baseline comparison within the exercise group

Women in the exercise group who adhered to the intervention protocol reported at baseline a statistically significant higher "Self-Control" subscale score (13.5 vs 12.4, p = 0.04) and a tendency of higher "Depressed mood score" (13.8 vs 12.8, p = 0.07), compared the non-adherent women in the exercise group.

Harms

No adverse events related to the intervention program or the assessments were registered in the ETIP trial. The woman in the control group who reported a score indicating suicidal risk (EDPS), got an immediate appointment with her general practitioner.

Discussion

Main findings

We found no statistically significant effect of offering supervised exercise training during pregnancy on psychological well-being in late pregnancy or three months postpartum, or on postnatal depression, among overweight and obese women. Both groups reported of good psychological well-being during pregnancy and postpartum, and had a low of risk for postnatal depression. The psychological well-being was stable during pregnancy and increased significantly from late pregnancy to postpartum in both groups. The women in the exercise group who adhered to the exercise protocol were characterized by higher self-control and fewer symptoms of depression at baseline, compared to the non-adherent women in the exercise group.

Strengths and weaknesses of the study

The major strength of this study was the randomised controlled design. We assessed well-being by valid and reliable questionnaires.[43,44] We included only women with pre-pregnancy overweight and obesity (BMI $\geq$ 28 kg/m^2) in the trial, contributing to a homogenous study group. We recorded exercise adherence as well as self-reported physical activity levels throughout the trial period in both groups.

The main limitations in the ETIP trial were a limited study sample, 20% dropout, and only 50% adherence to the exercise protocol.[32] These factors limit the chance of estimating an exact effect of exercise training on psychological well-being. Furthermore, a relatively high level of physical activity reported by the control group might have reduced the chance of finding an effect of the intervention. Our trial included comprehensive health assessments and close monitoring of the women, regardless of group allocation. This close follow-up by health personnel may have prevented reduced psychological well-being among all the women in the

trial. We had no information on previous mental health history or use of antidepressant treatment among the participants.

Comparison with other trials

Observational studies show that women who are physically active during pregnancy report better psychological well-being than less active women[28] and that the risk of psychological health problems increases in parallel to decreased exercise frequency during pregnancy.[27] A limited number of RCTs have investigated the effects of exercise training in pregnancy on psychological well-being, and the results diverge.[29,30,45] Bogaerts and colleagues[30] showed reduced anxiety in late pregnancy among obese women who received an intervention combining regular motivational interviewing with advice about healthy eating and physical activity in pregnancy, compared to advice only or a standard care control group. They found, however, no effect of the intervention on depression.[30] In our study, the level of anxiety did not differ between groups in late pregnancy, but we observed a tendency of less symptoms of anxiety among the women who exercised per-protocol compared to the control group, which indicates a positive effect of regular exercise during pregnancy on risk of anxiety. Gustafsson and co-workers[29] investigated the effect of regular exercise during pregnancy on late pregnancy psychological well-being assessed by PGWBI. They included women in all BMI categories, but found, similar to our trial, no effect of exercise on mental health. In their trial, as in ours, the participants reported of good psychological well-being at baseline, contrast to previous studies showing a high prevalence (15-25%) of depression and anxiety among overweight and obese pregnant women[2,7,8,46-49] and that especially the levels of anxiety increases from early to late pregnancy in this population.[47] Compared to the general population of overweight and obese women, more women in our trial reported to fulfil the recommendations for physical activity during and after pregnancy,[32] the number of pregnancy complications were lower, and number of women exceeding the Institute of Medicine guidelines for gestational weight gain

was also lower.[32,33] All these factors are associated with increased risk for reduced psychological well-being and could therefore explain stabile PGWBI scores during pregnancy in our study group. Again, this indicates that we included overweight and obese women with good psychological well-being in our trial.

We found no effect of exercise training on the risk for postnatal depression, which is in line with previous studies suggesting limited effect of exercise interventions during pregnancy on risk for depression after delivery.[31,45] Our results show that few women who participated in the trial reported of symptoms of postnatal depression. This is in contrast to a systematic review and meta-analysis reporting a high risk of developing depression during the postpartum period for women with pre-pregnancy obesity.[1] Also a cohort study by Ertel and collegues,[5] who assessed postnatal depression among 1686 women in all BMI categories, found that pre-pregnancy BMI >30 was associated with increased risk for depression six months postpartum. The EDPS collects the woman's self-perceived psychological well-being during the last week, and thereby the woman's current state of anxiety and depression. On the other hand, the "State and Trait Anxiety Inventory (STAI)" questionnaire, assesses both short-term and long-term symptoms, and might provide a different set of information compared to the EDPS. Even though the EDPS is the most frequently used questionnaire for assessing risk for depression postpartum, the type of questionnaires used in studies differs and this hampers comparison between trials.

Generalizability and clinical implications

When compared to women in the Norwegian Medical Birth Registry,[50] the ETIP population is representative for Norwegian overweight and obese pregnant women, according to BMI, obesity grades I, II, III, age, education, parity and occupational activity/employment.[32] However, it is likely to believe that women who volunteered for participation in an exercise trial are extra aware of possible benefits of maternal exercise, are more experienced with physical activity and suffer from less pregnancy complications. We believe that the findings in

our trial may be generalizable to relatively healthy pregnant women with pre-pregnancy BMI of 28 or more.

We based the trial intervention program on current recommendations for maternal exercise and designed it for easy implementation into clinical practice. Health care professionals, especially general practitioners and midwifes who consult pregnant women, are in a unique position to inform, help and guide overweight and obese women throughout pregnancy. Clear recommendations for exercise and physical activity should be given to all pregnant women, and the women should be closely monitored and motivated by maternal health care personnel throughout pregnancy. Assessing psychological well-being early in pregnancy may be important for prediction of adherence to exercise during pregnancy.

Conclusion

We found no statistically significant effects of supervised exercise training during pregnancy on psychological well-being in late pregnancy or postpartum, nor on the prevalence of postnatal depression, among overweight and obese women. Both groups reported good psychological well-being and low risk for postnatal depression. The level of self-control early in pregnancy may be important for exercise adherence during pregnancy. We need more research on the preventive effect of exercise during pregnancy on maternal well-being, and on the factors associated with motivation for exercise during pregnancy.

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Author Contributions: KKG acquired the data, analysed the data, interpreted the data and drafted the manuscript. ASH interpreted the data and critically revised the manuscript. SM designed the study and critically revised the manuscript, SNS designed the study and critically revised the manuscript, KÅS designed the study and critically revised the manuscript, TM acquired some of the data, deigned the study and critically revised the manuscript. All authors have approved the final version of the manuscript and are accountable for all aspects of the work.

Full trial protocol at https://www.ncbi.nlm.nih.gov/pubmed/21682869

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Figure legends

Figure 1. Changes in the PGWBI global score and the six subscales from baseline to late pregnancy in the exercise group and the control group. Data are means with 95% confidence intervals.

Figure 2. Changes in the PGWBI global score and the six subscales from late pregnancy to postpartum in the exercise group and the control group. Data are means with 95% confidence intervals.

Figure 1.

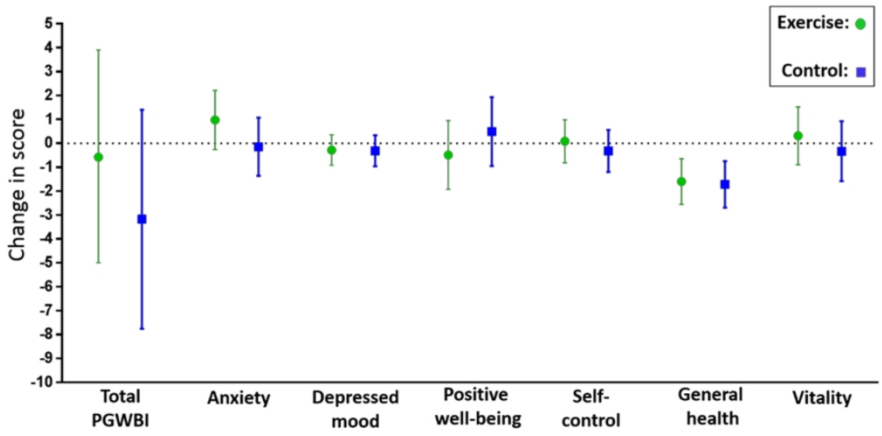

Figure 1. Change in the PGWBI global score and the six subscales from baseline to late pregnancy in the exercise group and the control group, presented as mean and 95% CI.

Figure 1. Change in the PGWBI global score and the six subscales from baseline to late pregnancy in the exercise group and the control group, presented as mean and 95% CI.

172x130mm (300 x 300 DPI)

Figure 2.

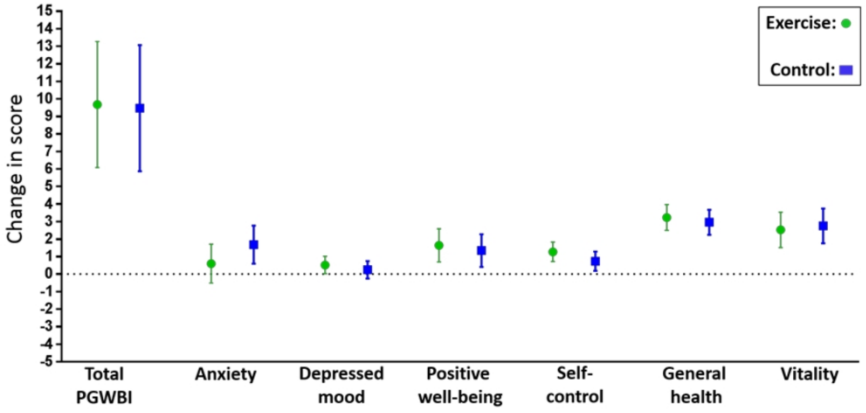

Figure 2. Change in the PGWBI global score and the six subscales from late pregnancy to three months postpartum in the exercise group and the control group, presented as mean and 95% CI.

Figure 2. Change in the PGWBI global score and the six subscales from late pregnancy to three months postpartum in the exercise group and the control group, presented as mean and 95% CI.

176x129mm (300 x 300 DPI)

Supplementary Table 1. Outcomes in PGWBI at late pregnancy and three months postpartum. "Per-protocol" model based analyses with comparison between groups presented as estimated mean difference, 95% confidence interval (CI) and *p*-value.

	Exercise Per protocol		**Control**		**Difference between groups**					
					Late pregnancy			**Postpartum**		
	Score late pregnancy N = 19	*Score postpartum N = 19*	*Score late pregnancy N = 36*	*Score postpartum N = 34*	*Diff*	*95% CI*	*P-value*	*Diff*	*95% CI*	*P-value*
Anxiety	21.4 (19.7, 23.2)	20.9 (19.3, 22.4)	19.5 (18.4, 20.7)	21.7 (20.7, 22.7)	1.88	-0.17, 3.93	0.07	-0.80	-2.66, 1.07	0.39
Depressed mood	13.6 (12.4, 14.3)	13.6 (12.8, 14.4)	13.2 (12.5, 13.8)	13.5 (12.9, 14.1)	0.20	-0.93, 1.33	0.72	0.14	-0.82, 1.10	0.77
Positive well-being	12.3 (11.0, 13.7)	14.2 (12.8, 15.6)	12.8 (11.9, 13.7)	13.9 (12.9, 14.8)	-0.41	-2.02, 1.24	0.62	0.36	-1.31, 2.03	0.66
Self-Control	13.2 (11.8, 14.6)	13.3 (12.4, 14.3)	12.1 (11.2, 13.0)	13.1 (12.5, 13.7)	1.05	-0.63, 2.73	0.21	0.18	-0.96, 1.32	0.75
General Health	8.5 (7.0, 10.0)	11.6 (10.4, 12.8)	8.1 (7.1, 9.1)	11.3 (10.5, 12.1)	0.45	-1.35, 2.25	0.62	0.31	-1.15, 1.76	0.67
Vitality	10.9 (9.0, 12.7)	12.0 (10.4, 13.6)	9.6 (8.4, 10.8)	12.3 (11.2, 13.4)	1.28	-0.96, 3.52	0.26	-0.29	-2.31, 1.74	0.77
PGWBI Index	80.2 (73.9, 86.6)	84.8 (79.5, 90.2)	74.7 (70.4, 79.0)	85.3 (81.5, 89.2)	5.55	-2.13, 13.2	0.15	-0.49	-7.18, 6.20	0.88

Missing late pregnancy: Exercise 6, control, 5. *Missing postpartum:* Exercise 5, control 4.
Statistics: General linear model analysis of covariance, with baseline mean as covariate in late pregnancy analyses, and late pregnancy mean as covariate in the postpartum analyses.
PGWBI: The Psychological General Well-Being Index (global score of all subscales).

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	5
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6-7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	5
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7-8
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7-8
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7-8
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7-8
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	7-8

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	9
	13b	For each group, losses and exclusions after randomisation, together with reasons	9
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9
	14b	Why the trial ended or was stopped	5
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	10
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	10, 12
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	11, 12, 13
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	11, 12, 13
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	13
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	14, 15
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	16, 17
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	17
Other information			
Registration	23	Registration number and name of trial registry	3
Protocol	24	Where the full trial protocol can be accessed, if available	18
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

Effects of supervised exercise training during pregnancy on psychological well-being among overweight and obese women, secondary analyses of the ETIP-trial, a randomized controlled trial.

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Keywords:	maternal obesity, MENTAL HEALTH, Depression & mood disorders < PSYCHIATRY, Anxiety disorders < PSYCHIATRY, Pregnancy and exercise responses, Maternal health, mental health, depression, anxiety, pregnancy complications

Effects of supervised exercise training during pregnancy on psychological well-being among overweight and obese women, secondary analyses of the ETIP-trial, a randomized controlled trial.

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Abstract

Objectives: Women with high body mass index (BMI) have increased risk for symptoms of anxiety and depression during pregnancy and postpartum. In this pre-specified secondary analysis from the Exercise Training in Pregnancy (ETIP) trial, our aim was to examine effects of supervised exercise during pregnancy on psychological well-being in late pregnancy and postpartum among women with a pre-pregnancy BMI ≥ 28 kg/m^2.

Design: Single-centre, parallel group, randomized controlled trial.

Setting: University Hospital, Norway

Participants: Ninety-one women (age 31.2±4.1 years, BMI 34.5±4.2 kg/m^2), 46 in the exercise group, 45 in the control group, were included in the trial.

Intervention: The exercise group was offered three weekly supervised exercise sessions (35 minutes of moderate intensity walking/running, and 25 minutes of resistance training), until delivery.

Primary and secondary outcomes measures: Primary analyses were based on intention to treat, with secondary per-protocol analyses. To assess psychological well-being, we used the «Psychological General Well-Being Index» (PGWBI) at inclusion (gw. 12-18), late pregnancy (gw. 34-37), and three months postpartum. Postpartum, we assessed depression using the «Edinburgh Postnatal Depression Scale» (EDPS).

Results: Numbers completed data collection: Late pregnancy 72 (exercise 38, control 36), postpartum 70 (exercise 36, control 34). In the exercise group, 50% adhered to the exercise protocol. Baseline PGWBI for all women was 76.4±12.6. Late pregnancy PGWBI; exercise 76.6 (95% CI 72.2, 81.0), control 74.0 (95% CI 69.4, 78.5) (p = 0.42). Postpartum PGWBI; exercise 85.4 (95% CI 81.9, 88.8), control 84.6 (95% CI 80.8, 88.4) (with no between-group difference, p = 0.77). There was no between-group difference in EDPS; exercise 2.96 (95% CI 1.7, 4.2), control 3.48 (95% CI 2.3, 4.7) (p = 0.55).

Conclusions: We found no effect of supervised exercise training during pregnancy on psychological well-being among women with high BMI. Our findings may be hampered by low adherence to the exercise protocol.

Trial registration number: ClinicalTrials.gov NCT01243554

Key words: Maternal health, mental health, depression, anxiety, pregnancy complications

Article summary

Strengths and limitations of this study:

- This study was a randomized controlled trial.
- The exercise program was supervised.
- The trial assessed psychological well-being at multiple time points; in early pregnancy, late pregnancy and three months postpartum
- The trial was limited by lower number of participants than originally planned.
- The trial was limited by relatively low adherence to the exercise intervention

Introduction

About 20% of pregnant women report of reduced psychological well-being and symptoms of depression and anxiety during pregnancy and postpartum.[1-3] The prevalence of reduced psychological well-being among pregnant women who are overweight and obese, are found to be even higher, about 30%.[1,2,4-8] Psychological well-being is for the purpose of this paper defined as "people's cognitive and affective evaluations of their lives; happiness, absence of negative emotions (e.g. depression, anxiety), satisfaction with life, and positive functioning".[9] Postnatal depression can be defined as "a type of clinical depression that occurs after childbirth".[10] Reduced psychological well-being may develop early in pregnancy, and symptoms of anxiety and depression in pregnancy or postpartum are associated with increased risk for complications e.g. hypertension, preterm birth, infant small for gestational age, lower rates of breastfeeding and impaired mother-newborn interaction.[11-15] These complications adds to other well documented maternal and foetal risks for in this population; such as gestational diabetes, maternal hypertension, pre-eclampsia and infants born large for gestational age.[16-21] Therefore, it is important to find strategies to prevent poor psychological well-being during pregnancy and the postpartum period.

Regular physical activity and supervised exercise training are beneficial for psychological well-being,[22-24] and contribute to reduced depressive symptoms among individuals who has been previously inactive.[24] Pregnant women are as the general population advised to perform regular exercise and be physically active,[25] but the frequency and intensity of exercise and physical activity tend to decline during pregnancy, especially among overweight and obese women.[26] Observational studies have found maternal exercise and physical activity to associate with better psychological well-being and reduced risk for postnatal depression.[27,28] However, results from randomized controlled trials (RCTs) on the effect of exercise training on psychological well-being diverge.[29-31]

In the Exercise Training in Pregnancy (ETIP) trial, we determined the effect of offering supervised exercise training during pregnancy on maternal and foetal outcomes among 91 women with overweight or obesity, with gestational weight gain as the primary outcome.[32-35] In this pre-specified[35] secondary analysis of the ETIP trial, we aimed to determine the effect of exercise training on self-perceived psychological well-being in late pregnancy and three months postpartum, and the effect of exercise training in pregnancy on the risk for postnatal depression.

Methods

Trial design

The ETIP trial was a single-centre, parallel-group RCT where we determined the effects of offering overweight and obese women supervised exercise training during pregnancy compared to standard maternal care only. The trial was undertaken at the Norwegian University of Science and Technology (NTNU) and St. Olavs hospital, Trondheim University Hospital, Norway. We started inclusion in September 2010, with the last assessments in November 2015. The ETIP trial protocol and detailed description of the methods have been published elsewhere.[32,35] The study was approved by the Regional Committee for Medical and Health Research Ethics (REK-midt 2010/1522) and registered in ClinicalTrials.gov (NCT01243554). The ETIP trial was submitted to Clinical Trials September 06, 2010 with the Study Start Date set to September 2010 (Please see attached PRS Review Comments). Clinical Trials responded with a comment that they wanted us to respond to and therefore did not release the trial immediately. Due to a delay at our Faculty's administration, the respond to the comment was not submitted until November 2010.

Participants

We included women with pre-pregnancy body mass index (BMI) ≥ 28 kg/m^2, ≥ 18 year, in gestational week 12-18, carrying a singleton live foetus at an 11–14 week ultrasound scan. Categorisation of overweight and obesity related to BMI, was based on the World Health Organization (WHO) classification system.[36] Pre-pregnancy BMI was based on self-reported information. Participants had to attend assessments and exercise classes at St. Olavs hospital. We excluded women with high risk of preterm birth, diseases that could interfere with participation, or if they exercised twice or more weekly in the period before inclusion. The women received written information and signed informed consent on behalf of themselves and their offspring before inclusion into the trial. We recruited participants through invitations sent along with notices for routine ultrasound scan appointments, information sent to general practitioners, and through Google advertisements. At the last study visit, the women received infant food worth 500 Norwegian kroner.

Intervention

All participants, regardless of group allocation, received maternity and postpartum care according to the Norwegian Standard Maternity Care for pregnant women, which is offered to all (free of charge).[37]

Women in the exercise group were offered supervised exercise sessions at St. Olavs hospital three times weekly from inclusion until delivery. The exercise program provided was in accordance with the recommendations from the American College of Obstetricians and Gynaecologists[25,38,39] and from the Norwegian Directorate of Health for physical activity during pregnancy.[40] The exercise sessions were supervised by a physical therapist and consisted of 35 minutes of treadmill walking at approximately 80% of maximal aerobic capacity (corresponding to Borg scale 12–15)[35] followed by 25 minutes of resistance training, including pelvic floor muscle training. In addition to the supervised program, we asked the women to exercise at home for 50 minutes at least once weekly, and to do daily pelvic floor muscle

exercises. For a full description of the exercise intervention, see previous reports (Supplemental File 1.).[32,35] Adherence to the exercise program was registered in a training diary. Women in the control group were not discouraged from physical activity or exercise.

Outcomes

Sociodemographic data was collected by self-reported questionnaires at baseline assessments. Information regarding the participants' psychological well-being and risk of postnatal depression was assessed by self-reported questionnaires, completed at the hospital while they underwent a 2 h oral glucose tolerance test at baseline, late pregnancy and three months postpartum, with trial researchers available to clarify questions if needed.

Psychological well-being was assessed by the "Psychological General Well-Being Index" (PGWBI) questionnaire (PGWBI © 1984 Harold J. Dupuy, Mapi Research Trust)[41,42] at baseline (gestational week 12-18), in late pregnancy (gestational week 34-37) and three months postpartum. The Psychological General Well-being (PGWB) scale measures the last week self-perceived psychological health and general well-being, and intends to assess health related quality of life or, said otherwise, to reflect a sense of well-being or distress that includes positive as well as negative intrapersonal affective or emotional states.[35] It consists of 22 items with a six-point self-response scale that ranges from zero (= most negative option) to five (= most positive option) and includes six non-overlapping dimensions: anxiety (five items), depressed mood (three items), positive well-being (four items), self-control (three items), general health (three items), and vitality (four items).[35, 38] Each dimension is summed and the total (maximum = 110) forms the overall PGWBI. The anxiety dimension assessed whether the subjects were bothered by nervousness, were generally tense, anxious, worried or upset, and/or under stress strain or pressure. Depressed-mood measured if the participants were depressed, hopeless, or downhearted and 'blue'. Positive well-being indicated the general spirit, cheerfulness, or happiness and satisfaction with personal life. The self-control dimension intended to measure

whether the subjects felt emotionally stable, in firm control, or afraid of losing control. General health assessed if the subjects were bothered with pain, disorder, or illness and whether they were healthy enough 'to do things.' Finally, vitality contained items that assessed the participants' energy, whether they felt active, vigorous, or sluggish, tired and worn out.[35]

The PGWBI questionnaire is a generic questionnaire frequent used in clinical trials across many conditions, and translated to several languages.[43-46] The PGWBI has been found suitable for subjects 14-90 years and is a highly preferred self-administered inventory.[35] The internal consistency reliability is high with Cronbach´s alpha correlations between 0.90 and 0.94.[35] Similar correlations (Cronbach´s alpha > 0.90) have been shown for tests done in Sweden,[43] with culture and language similar to the Norwegian,[44] and recently used by Gustafsson and colleges in a clinical trial among Norwegian pregnant women.[29] The present Norwegian version of the questionnaire was translated by a standard forward-backward method at St. Olavs Hospital, the university Hospital, Trondheim, Norway, in February 2002.[47]

To measure the prevalence of symptoms of postnatal depression, the participants also completed the "Edinburgh Postnatal Depression Scale" (EPDS) questionnaire (Cox, Holden and Sagosky, 1987).[48] The questionnaire is a non-generic self-rating scale, which measures the presence of depressive symptoms during in the postpartum period, indicating how the mother has felt during the last week.[48,49] The EPDS questionnaire contains 10 questions. All questions contain four response alternatives were the women are asked to "please underline the answer witch comes closest to how you have felt in the past 7 days".[48] We estimated total score of the ten items with use of a scoring system 0-3, with "0" representing the most negative option, and "3" the most positive option. Based on validations of the questionnaire,[48] we used a cut-off score of ≥ 10 indicating minor depression, ≥ 13 indicating a major depression. The EPDS questionnaire is developed and commonly used for measurement of depressive symptoms in the postpartum period, but is also used and validated for the pregnancy period.[48] The

questionnaire is translated to Norwegian and found valid to detect postpartum depression in a Norwegian population.[50,51]

Additionally, the participants reported their self-perceived general health status at baseline and in late pregnancy as either "very good", "good", "either good or bad", "quite bad" or "bad". This question is taken from the SF 36 Short Form Health Survey. This survey is translated to Norwegian, and tested for reliability and validity in a Norwegian population.

Sample size

The sample size calculation for the ETIP trial was based on difference between groups in the primary outcome, gestational weight gain from baseline assessments to delivery (Supplemental File 1.).[32,35] Based on previous studies, a mean change of 6 kg was assumed as clinical relevant.[52,53] A two-sided independent sample *t*-test with a 5 % level of significance, a standard deviation of 10, and a power of 0.90 defined our target study population to be 59 in each group. We estimated the dropout rate in the trial to be 15 %, and on basis of these estimations aimed to include 150 women. We have not performed a separate power calculation for the secondary analyses reported in this paper.

Randomization and blinding

Randomisation was performed after baseline assessments using a computer random number generator, developed and administrated at the Unit for Applied Clinical Research, NTNU. The personnel who provided the participants with questionnaires regarding psychological well-being in late pregnancy and postpartum were not blinded for group allocation. Further details about randomization and blinding in the ETIP trial are published previously.[32]

Statistical methods

We confirmed baseline data normality using Shapiro-Wilk tests and visual inspection of plots and histograms. Comparisons between groups at baseline was analysed by independent samples t-tests and Fisher's Exact tests. We analysed between-groups differences in the effect of exercise training on psychological well-being (assessed by PGWBI) in late pregnancy and postpartum, and between-groups difference in "Self-perceived general health status" late pregnancy by general linear model analysis of covariance. Changes within-groups from baseline to late pregnancy and from late pregnancy to postpartum were also analysed by general linear model analysis of covariance. Baseline values were set as a covariate at late pregnancy analyses, and late pregnancy values were set as covariates at postpartum analyses. We analysed differences between groups in EDPS using an independent samples t-test. We assessed differences in baseline PGWBI between the participants who exercised per protocol and the non-adherent participants in the exercise group by independent samples t-tests. Due to the randomisation model, we assumed no systematic differences between groups at baseline. We based our primary analyses on the principle "intention to treat" and additionally performed "per protocol" analyses, according to pre-specified cut-off values for adherence to the exercise program (Supplemental File 1.).[35] No adjustment for multiple testing have been undertaken.

We used IBM SPSS Statistics 23. We consider *P*-values < 0.05 as statistically significant.

Patient and public involvement

No patients involved.

Results

We assessed 136 women for eligibility and included 91 women, with 46 in the exercise group and 45 in the control group. Figure 1 shows the participant flow in the ETIP trial. . The exercise group exercised 31.7 ± 15.3 (range 0-53) sessions at the hospital and 19.2 ± 16.5 (range 0-72) sessions at home, giving a weekly average of 1.30 ± 0.8 supervised sessions and 0.8 ± 0.7 home-based sessions. About 50% (n=19) of the women in the exercise group exercised according to our pre-specified cut-off values for per protocol analyses.

Table 1 shows the baseline characteristics of the participants. There were no statistically significant differences between the groups at baseline. Full trial baseline data have been published previously.[32] At inclusion, 55% in the exercise group and 53% in the control group reported to fulfil the recommendations for physical activity (≥ 150 min/week of moderate intensity physical activity).

In late pregnancy, 61% in the exercise group and 66% in the control group reported to adhere to the recommendations for physical activity, with corresponding numbers postpartum being 72% in the exercise group and 79% in the control group. In late pregnancy, 77% in the exercise group compared to 23% in the control group ($p < 0.01$) reported regular exercise, with corresponding numbers postpartum being 46% in the exercise group and 25% in the control group ($p = 0.16$). About 58% in exercise group and 44% in the control group (between-group difference, $p = 0.35$) gained more weight during pregnancy than recommended by the Institute of Medicine.[54]

Table 1. Subjects characteristics at baseline for the exercise and the control group. Observed data are presented as means ± standard deviation, or number of participants with percentages. Psychological well-being is presented with the Psychological General Well-Being Index (PGWBI) global score and six subscales.

Subjects characteristics	**Exercise Group (*n* = 46)**	**Control Group (*n* = 45)**
	Mean ± SD/N (%)	*Mean ± SD/N (%)*
Age (years)	31.3 ± 3.8	31.4 ± 4.7
Body weight (kg)	95.3 ± 12.8	98.3 ± 14.2
Body mass index (kg/m²)	33.9 ± 3.8	35.1 ± 4.6
Weight classification		
Overweight, BMI 28.0–29.9 kg/m²	3 (6.6)	5 (11.1)
Class 1 obesity, BMI 30.0–34.9 kg/m²	28 (62.2)	19 (42.2)
Class 2 obesity, BMI 35.0–39.9 kg/m²	11 (24.4)	15 (33.3)
Class 3 obesity, BMI ≥ 40.0 kg/m²	3 (6.6)	6 (13.3)
Parity		
0	22 (47.8)	19 (42.2)
1	19 (41.3)	19 (42.2)
2	5 (10.9)	4 (8.9)
≥3	0 (0.0)	3 (6.7)
Current smoking	2 (4.7)	4 (8.9)
Education		
Primary/secondary school	1 (2.3)	3 (7.0)
High school	15 (34.1)	12 (27.9)
University ≤4 years	14 (31.8)	11 (25.6)
University >4 years	14 (31.8)	17 (39.5)
Currently employed	38 (82.6)	33 (73.3)
Self-perceived general health status		
Very good	0 (0.0)	4 (9.3)
Good	25 (54.3)	19 (49.4)
Either good or bad	18 (39.1)	20 (46.5)
Quite bad	3 (6.5)	0 (0.0)
Bad	0 (0.0)	0 (0.0)
Psychological General Well-Being Index (PGWBI)	76.6±11.1	76.2±14.3
Anxiety	19.8±3.3	19.2±4.6
Depressed mood	13.2±1.9	13.2±1.9
Positive well-being	12.2±2.8	12.6±3.1
Self-Control	12.9±1.7	12.0±2.5
General Health	9.7±2.8	9.5±2.7
Vitality	8.8±3.8	10.1±3.4

Missing: Education: Control: 1. General health status: Control: 3. PGWBI: Exercise; 2, control; 4.
Statistics: Baseline variables were analysed by Independent samples t-test, and Fisher's Exact Test.

Psychological well-being in late pregnancy

We did not find any statistically significant difference between the groups in PGWBI global score, or in any of the six subscales, in late pregnancy (Table 2). The late pregnancy per-protocol analyses showed PGWBI global score of 80.2 (95% CI 73.9, 86.6) in the exercise group, and 74.7 (95% CI 70.4, 79.0) in the control group ($p = 0.15$) (Supplementary Table 1). No statistically significant difference between the exercise per-protocol group and the control group were found, but we observed a tendency of higher "Anxiety" score in the per-protocol exercise group (21.4) compared to the control group (19.5) ($p = 0.07$) (Supplementary Table 1). Figure 2 illustrates the changes in PGWBI global score and subscales from baseline to late pregnancy in each group.

Self-perceived general health status in late pregnancy was reported to be "Very good" by 9% in the exercise group and 11% in the control group, "Good" by 53% in the exercise group and 29% in the control group, "Either good or bad" by 21% in the exercise group and 50%, "Quite bad" by 15% in the exercise group and 11% in the control group, and "Bad" by 3% in the exercise group and none in the control group (between-group difference, $p = 0.37$). Results were similar in the per-protocol analyses.

Psychological well-being three months postpartum

We did not find any statistically significant difference between the groups in PGWBI global score, or in any of the six subscales three months postpartum (Table 2). The postpartum per-protocol analyses showed PGWBI global score of 84.8 (95% CI 79.5, 90.2) in the exercise group, and 85.3 (95% CI 81.5, 89.2) in the control group ($p = 0.88$), with no statistically

significant differences in any of the six subscales (Supplementary Table 1). Figure 3 illustrates the changes in PGWBI global score and subscales from late pregnancy to postpartum in each group.

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290 **Table 2.** Psychological general well-being (PGWBI), global score and subscales, in late pregnancy and three months postpartum. "Intention to
291 treat" model based analyses with comparisons between groups presented as estimated mean difference with 95% confidence intervals (CI) and *p*-
292 values.

	All participants	**Exercise**		**Control**		**Difference between groups**					
						Late pregnancy			**Postpartum**		
	Score at baseline N = 91	*Score late pregnancy N = 38*	*Score postpartum N = 36*	*Score late pregnancy N = 36*	*Score postpartum N = 34*	*Diff*	*95% CI*	*P-value*	*Diff*	*95% CI*	*P-value*
PGWBI	77.2	76.6 (72.2, 81.0)	85.4 (81.9, 88.8)	74.0 (69.4, 78.5)	84.6 (80.8, 88.4)	2.60	-3.77, 8.97	0.42	0. 77	-4.42, 5.95	0.77
Anxiety	19.7	20.7 (19.5, 22.0)	20.6 (19.5, 21.7)	19.6 (18.4, 20.8)	21.8 (20.7, 23.0)	1.12	-0.61, 2.86	0.20	-1.26	-2.98, 0.37	0.13
Depressed mood	13.4	13.2 (12.5, 13.8)	13.7 (13.2, 14.1)	13.1 (12.5, 13.8)	13.4 (12.9, 13.9)	-0.03	-0.88, 0.94	0.95	0.25	-0.43, 0.93	0.47
Positive well-being	12.5	12.0 (11.0, 13.0)	13.9 (13.0, 14.9)	12.5 (11.5, 13.5)	13.6 (12.7, 14.6)	-0.49	-1.93, 0.95	0.50	0.27	-1.07, 1.61	0.68
Self-Control	12.5	12.6 (11.7, 13.5)	13.6 (13.0, 14.1)	12.2 (11.3, 13.1)	13.1 (12.5, 13.7)	0.40	-0.87, 1.67	0.53	0.44	-0.38, 1.25	0.29
General Health	9.7	8.1 (7.1, 9.0)	11.5 (10.8, 12.2)	8.0 (7.0, 8.9)	11.2 (10.5, 11.9)	0.12	-1.24, 1.49	0.86	0.31	-0.72, 1.33	0.55
Vitality	9.5	9.8 (8.6, 11.0)	12.4 (11.3, 13.4)	9.2 (7.9, 10.4)	12.0 (10.9, 13.1)	0.65	-1.15, 2.44	0.47	0.38	-1.18, 1.94	0.63

Missing late pregnancy: Exercise 8, control, 5. *Missing postpartum:* Exercise 7, control 4.
Statistics: General linear model analysis of covariance with baseline mean and late pregnancy mean as covariates.
PGWBI = The Psychological General Well-Being Index (global score of all subscales).

Postnatal depression

We found no statistically significant difference in total EPSD score three months postpartum between the exercise (2.96, 95% CI 1.7, 4.2) and control group (3.48, 95% CI 2.3, 4.7) (p = 0.55). No women in either the exercise group or the control group reported of a total EPSD score of 13 or more, representing indication of major depression. Two women (7.1%) in the exercise group and three women (10.3%) in the control group reported at total EPSD score between 10 and 12, representing indication of a minor depression. When analysing per-protocol, no statistical significant difference in total EPDS score was found between the exercise group (2.38, 95% CI 1.72, 4.2) and the control group (3.48, 95% CI 2.3, 4.7) (p = 0.30).

Baseline comparison within the exercise group

Women in the exercise group who adhered to the intervention protocol reported at baseline a statistically significant higher "Self-Control" subscale score (13.5 vs 12.4, p = 0.04) and a tendency of higher "Depressed mood score" (13.8 vs 12.8, p = 0.07), compared the non-adherent women in the exercise group.

Harms

No adverse events related to the intervention program or the assessments were registered in the ETIP trial. The woman in the control group, who reported a score indicating suicidal risk (EDPS), got an immediate appointment with her general practitioner.

Discussion

Main findings

We found no statistically significant effect of offering supervised exercise training during pregnancy on psychological well-being in late pregnancy or three months postpartum, or on symptoms of postnatal depression, among women who are overweight or obese. Both groups reported of good psychological well-being during pregnancy and postpartum, and had a low of risk for postnatal depression. The psychological well-being was stable during pregnancy and increased significantly from late pregnancy to postpartum in both groups. The women in the exercise group who adhered to the exercise protocol were characterized by higher self-control and fewer symptoms of depression at baseline, compared to the non-adherent women in the exercise group. Only 50% of the women in the exercise group followed the exercise-protocol, and we included less participants than estimated in the trial protocol.

Strengths and weaknesses of the study

The major strength of this study was the randomised controlled design. We assessed well-being by valid and reliable questionnaires.[55,56] We included only women with pre-pregnancy overweight and obesity (BMI $\geq$ 28 kg/m^2) in the trial, contributing to a homogenous study group. We recorded exercise adherence as well as self-reported physical activity levels throughout the trial period in both groups.

The main limitations in the ETIP trial were a limited study sample, 20% dropout, and only 50% adherence to the exercise protocol.[32] The low adherence to the exercise protocol may be explained by discomfort, especially in the first trimester, by the women being anxious to be exhausted, by having trouble with prioritizing time for exercise, and by having lack of motivation for life-style changes.

These factors limit the chance of estimating an exact effect of exercise training on psychological well-being. Furthermore, a relatively high level of physical activity reported by

the control group might have reduced the chance of finding an effect of the intervention. Our trial included comprehensive health assessments and close monitoring of the women, regardless of group allocation. This close follow-up by health personnel may have prevented reduced psychological well-being among all the women in the trial. We had no information on previous mental health history or use of antidepressant treatment among the participants.

Comparison with other trials

Observational studies show that women who are physically active during pregnancy report better psychological well-being than less active women[28] and that the risk of psychological health problems increases in parallel to decreased exercise frequency during pregnancy.[27] A limited number of RCTs have investigated the effects of exercise training in pregnancy on psychological well-being, and the results diverge.[29,30,57] Bogaerts and colleagues[30] showed reduced anxiety in late pregnancy among obese women who received an intervention combining regular motivational interviewing with advice about healthy eating and physical activity in pregnancy, compared to advice only or a standard care control group. They found, however, no effect of the intervention on depression.[30] In our study, the level of anxiety did not differ between groups in late pregnancy, but we observed a tendency of less symptoms of anxiety among the women who exercised per-protocol compared to the control group, which indicates a positive effect of regular exercise during pregnancy on risk of anxiety. Gustafsson and co-workers[29] investigated the effect of regular exercise during pregnancy on late pregnancy psychological well-being assessed by PGWBI. They included women in all BMI categories, but found, similar to our trial, no effect of exercise on mental health. In their trial, as in ours, the participants reported of good psychological well-being at baseline, contrast to previous studies showing a high prevalence (15-25%) of depression and anxiety among overweight and obese pregnant women[2,7,8,58-61] and that especially the levels of anxiety increases from early to late pregnancy in this population.[59] Compared to the general population of women who are

overweight or obese, more women in our trial reported to fulfil the recommendations for physical activity during and after pregnancy,[32] the number of pregnancy complications were lower, and number of women exceeding the Institute of Medicine guidelines for gestational weight gain was also lower.[32,33] All these factors are associated with increased risk for reduced psychological well-being and could therefore explain stabile PGWBI scores during pregnancy in our study group. Again, this indicates that we included women with good psychological well-being in our trial.

We found no effect of exercise training on the risk for postnatal depression, which is in line with previous studies suggesting limited effect of exercise interventions during pregnancy on risk for depression after delivery.[31,57] Our results show that few women who participated in the trial reported of symptoms of postnatal depression. This is in contrast to a systematic review and meta-analysis reporting a high risk of developing depression during the postpartum period for women with pre-pregnancy obesity.[1] Also a cohort study by Ertel and collegues,[5] who assessed postnatal depression among 1686 women in all BMI categories, found that pre-pregnancy BMI >30 was associated with increased risk for depression six months postpartum. The EDPS collects the woman's self-perceived psychological well-being during the last week, and thereby the woman's current state of anxiety and depression. On the other hand, the "State and Trait Anxiety Inventory (STAI)" questionnaire, assesses both short-term and long-term symptoms, and might provide a different set of information compared to the EDPS. Even though the EDPS is the most frequently used questionnaire for assessing risk for depression postpartum, the type of questionnaires used in studies differs and this hampers comparison between trials.

Generalizability and clinical implications

When compared to women in the Norwegian Medical Birth Registry,[62] the ETIP population is representative for Norwegian overweight and obese pregnant women, according to BMI, obesity grades I, II, III, age, education, parity and occupational activity/employment.[32]

However, it is likely to believe that women who volunteered for participation in an exercise trial are extra aware of possible benefits of maternal exercise, are more experienced with physical activity and suffer from less pregnancy complications. We believe that the findings in our trial may be generalizable to relatively healthy pregnant women with pre-pregnancy BMI of 28 or more.

We based the trial intervention program on current recommendations for maternal exercise and designed it for easy implementation into clinical practice. Health care professionals, especially general practitioners and midwifes who consult pregnant women, are in a unique position to inform, help and guide women with high BMI throughout pregnancy. Clear recommendations for exercise and physical activity should be given to all pregnant women, and the women should be closely monitored and motivated by maternal health care personnel throughout pregnancy. Assessing psychological well-being early in pregnancy may be important for prediction of adherence to exercise during pregnancy.

Conclusion

We found no statistically significant effects of supervised exercise training during pregnancy on psychological well-being in late pregnancy or postpartum, nor on the prevalence of symptoms of postnatal depression, among women with overweight or obese women. Both groups reported good psychological well-being and low risk for postnatal depression. The level of self-control early in pregnancy may be important for exercise adherence during pregnancy. Low adherence to the exercise protocol may have reduced the chance of finding an effect of regular maternal exercise on mental health.

We need high sample-size trials with sufficient adherence to intervention protocols to be able to investigate the true effect of exercise during pregnancy on maternal well-being, and to examine factors associated with motivation for exercise during pregnancy.

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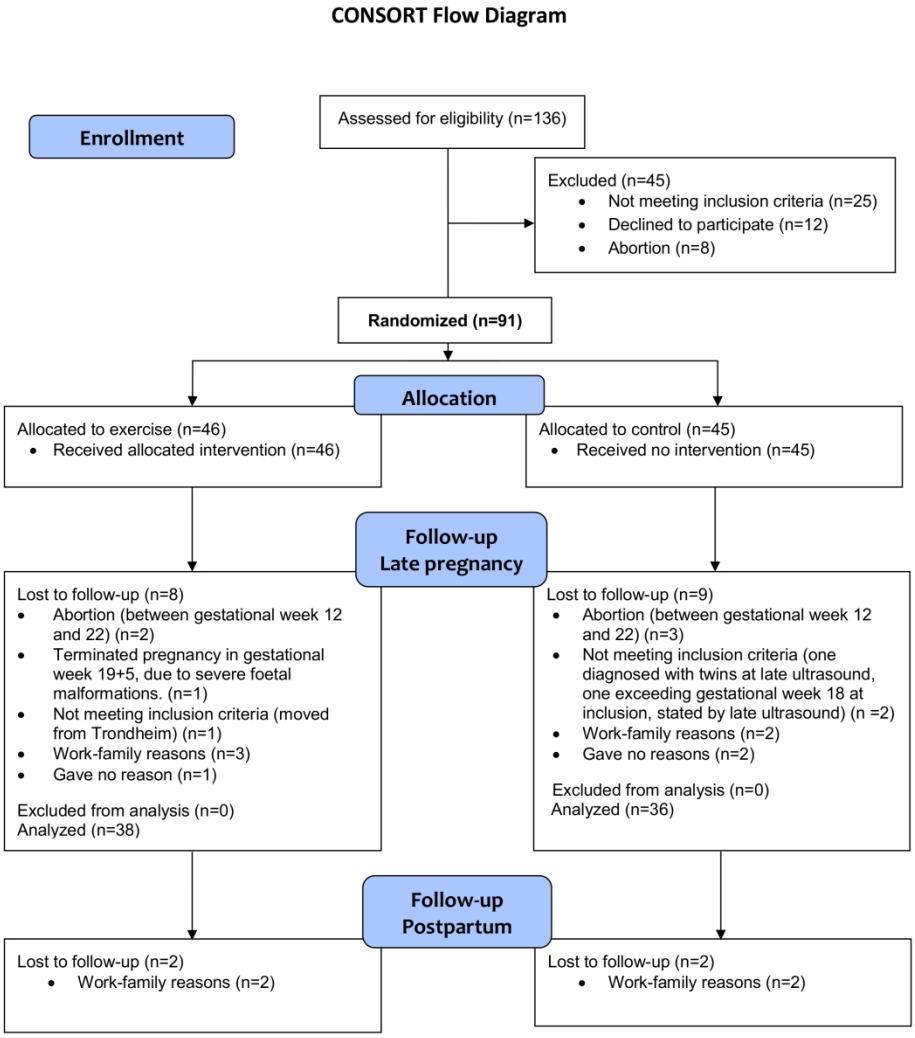
Figure legends

Figure 1. CONSORT flow chart ETIP trial.

Figure 2. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from baseline to late pregnancy in the exercise group and the control group. Data are means with 95% confidence intervals.

Figure 3. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from late pregnancy to postpartum in the exercise group and the control group. Data are means with 95% confidence intervals.



CONSORT Flow chart ETIP trial

209x229mm (300 x 300 DPI)

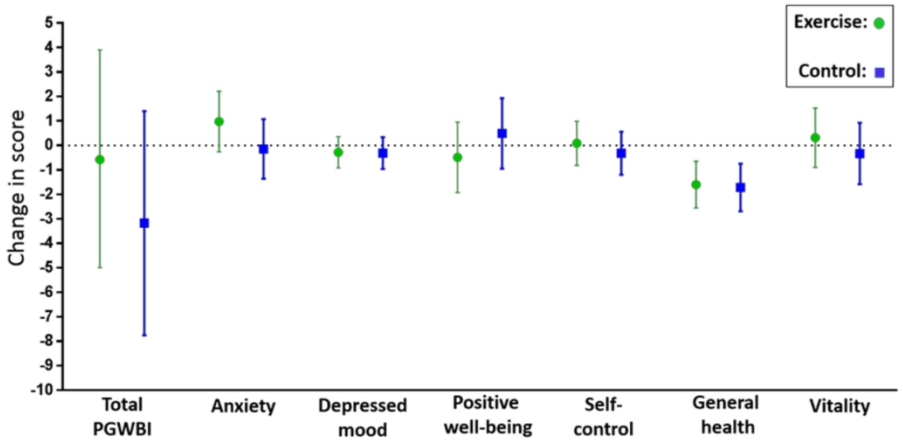


Figure 2. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from baseline to late pregnancy in the exercise group and the control group. Data are means with 95% confidence intervals.

168x88mm (300 x 300 DPI)

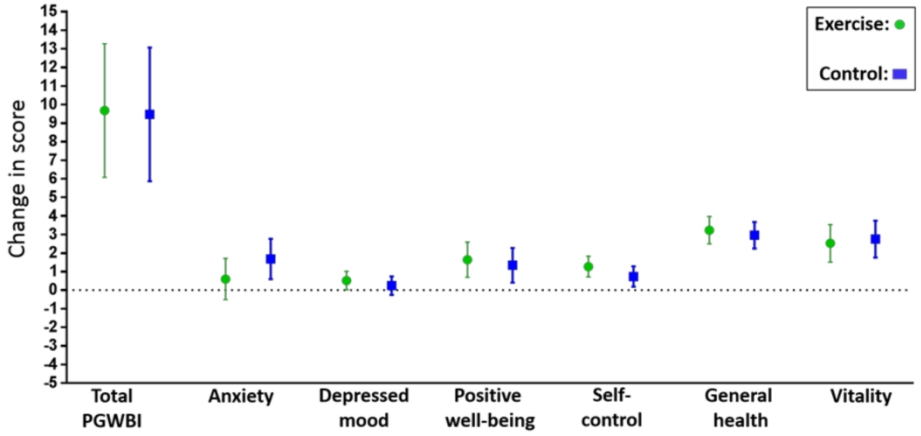


Figure 3. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from late pregnancy to postpartum in the exercise group and the control group. Data are means with 95% confidence intervals.

166x88mm (300 x 300 DPI)

Supplementary Table 1. Outcomes in PGWBI at late pregnancy and three months postpartum. "Per-protocol" model based analyses with comparison between groups presented as estimated mean difference, 95% confidence interval (CI) and *p*-value.

	Exercise Per protocol		**Control**		**Difference between groups**					
					Late pregnancy			**Postpartum**		
	Score late pregnancy N = 19	*Score postpartum N = 19*	*Score late pregnancy N = 36*	*Score postpartum N = 34*	*Diff*	*95% CI*	*P-value*	*Diff*	*95% CI*	*P-value*
Anxiety	21.4 (19.7, 23.2)	20.9 (19.3, 22.4)	19.5 (18.4, 20.7)	21.7 (20.7, 22.7)	1.88	-0.17, 3.93	0.07	-0.80	-2.66, 1.07	0.39
Depressed mood	13.6 (12.4, 14.3)	13.6 (12.8, 14.4)	13.2 (12.5, 13.8)	13.5 (12.9, 14.1)	0.20	-0.93, 1.33	0.72	0.14	-0.82, 1.10	0.77
Positive well-being	12.3 (11.0, 13.7)	14.2 (12.8, 15.6)	12.8 (11.9, 13.7)	13.9 (12.9, 14.8)	-0.41	-2.02, 1.24	0.62	0.36	-1.31, 2.03	0.66
Self-Control	13.2 (11.8, 14.6)	13.3 (12.4, 14.3)	12.1 (11.2, 13.0)	13.1 (12.5, 13.7)	1.05	-0.63, 2.73	0.21	0.18	-0.96, 1.32	0.75
General Health	8.5 (7.0, 10.0)	11.6 (10.4, 12.8)	8.1 (7.1, 9.1)	11.3 (10.5, 12.1)	0.45	-1.35, 2.25	0.62	0.31	-1.15, 1.76	0.67
Vitality	10.9 (9.0, 12.7)	12.0 (10.4, 13.6)	9.6 (8.4, 10.8)	12.3 (11.2, 13.4)	1.28	-0.96, 3.52	0.26	-0.29	-2.31, 1.74	0.77
PGWBI Index	80.2 (73.9, 86.6)	84.8 (79.5, 90.2)	74.7 (70.4, 79.0)	85.3 (81.5, 89.2)	5.55	-2.13, 13.2	0.15	-0.49	-7.18, 6.20	0.88

Missing late pregnancy: Exercise 6, control, 5. *Missing postpartum:* Exercise 5, control 4.
Statistics: General linear model analysis of covariance, with baseline mean as covariate in late pregnancy analyses, and late pregnancy mean as covariate in the postpartum analyses.
PGWBI: The Psychological General Well-Being Index (global score of all subscales).

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	5
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6-7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	5
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7-8
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7-8
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7-8
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7-8
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	7-8

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	9
	13b	For each group, losses and exclusions after randomisation, together with reasons	9
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9
	14b	Why the trial ended or was stopped	5
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	10
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	10, 12
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	11, 12, 13
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	11, 12, 13
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	13
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	14, 15
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	16, 17
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	17
Other information			
Registration	23	Registration number and name of trial registry	3
Protocol	24	Where the full trial protocol can be accessed, if available	18
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

Effects of supervised exercise training during pregnancy on psychological well-being among overweight and obese women: Secondary analyses of the ETIP-trial, a randomized controlled trial.

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Effects of supervised exercise training during pregnancy on psychological well-being among overweight and obese women: Secondary analyses of the ETIP-trial, a randomized controlled trial.

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Abstract

Objectives: Women with high body mass index (BMI) have increased risk for symptoms of anxiety and depression during pregnancy and postpartum. In this pre-specified secondary analysis from the ETIP trial, our aim was to examine effects of supervised exercise during pregnancy on psychological well-being in late pregnancy and postpartum among women with a pre-pregnancy BMI ≥ 28 kg/m^2.

Design: Single-centre, parallel group, randomized controlled trial.

Setting: University Hospital, Norway

Participants: Ninety-one women (age 31.2±4.1 years, BMI 34.5±4.2 kg/m^2), 46 in the exercise group, 45 in the control group, were included in the trial.

Intervention: The exercise group was offered three weekly supervised exercise sessions (35 minutes of moderate intensity walking/running and 25 minutes of resistance training), until delivery.

Primary and secondary outcomes measures: Primary analyses were based on intention to treat, with secondary per-protocol analyses. To assess psychological well-being, we used the «Psychological General Well-Being Index» (PGWBI) at inclusion (gestational week 12-18), late pregnancy (gestational week 34-37), and three months postpartum. We assessed postpartum depression using the «Edinburgh Postnatal Depression Scale» (EDPS).

Results: Numbers completed data collection: Late pregnancy 72 (exercise 38, control 36), postpartum 70 (exercise 36, control 34). In the exercise group, 50% adhered to the exercise protocol. Baseline PGWBI for all women was 76.4±12.6. Late pregnancy PGWBI; exercise 76.6 (95% CI 72.2, 81.0), control 74.0 (95% CI 69.4, 78.5) (p = 0.42). Postpartum PGWBI; exercise 85.4 (95% CI 81.9, 88.8), control 84.6 (95% CI 80.8, 88.4) (with no between-group difference, p = 0.77). There was no between-group difference in EDPS; exercise 2.96 (95% CI 1.7, 4.2), control 3.48 (95% CI 2.3, 4.7) (p = 0.55).

Conclusions: We found no effect of supervised exercise during pregnancy on psychological well-being among women with high BMI. Our findings may be hampered by low adherence to the exercise protocol.

Trial registration number: ClinicalTrials.gov NCT01243554

Key words: Maternal health, mental health, depression, anxiety, pregnancy complications

Article summary

Strengths and limitations of this study:

- This study was a randomized controlled trial.
- The exercise program was supervised.
- The trial assessed psychological well-being at multiple time points; in early pregnancy, late pregnancy and three months postpartum.
- The trial was limited by a lower number of participants than originally planned.
- The trial was limited by relatively low adherence to the exercise intervention.

Introduction

About 20% of pregnant women report reduced psychological well-being and symptoms of depression and anxiety during pregnancy and postpartum.[1-3] The prevalence of reduced psychological well-being among pregnant women who are overweight and obese is found to be even higher; about 30%.[1,2,4-8] For the purpose of this paper, psychological well-being is defined as "people's cognitive and affective evaluations of their lives; happiness, absence of negative emotions (e.g. depression, anxiety), satisfaction with life, and positive functioning".[9] Postnatal depression can be defined as "a type of clinical depression that occurs after childbirth".[10] Reduced psychological well-being may develop early in pregnancy and symptoms of anxiety and depression in pregnancy or postpartum are associated with increased risk for complications, e.g. hypertension, preterm birth, infant small for gestational age, lower rates of breastfeeding and impaired mother-newborn interaction.[11-15] These complications adds to other well-documented maternal and foetal risks for women with obesity; such as gestational diabetes, maternal hypertension, pre-eclampsia and infants born large for gestational age.[16-21] Therefore, it is important to find strategies to prevent poor psychological well-being during pregnancy and the postpartum period for women with obesity.

Regular physical activity and/or supervised exercise training is beneficial for psychological well-being,[22-24] and contributes to reduced depressive symptoms among previously inactive individuals.[24] Pregnant women are, equal to the general population, advised to perform regular exercise and be physically active,[25] but the frequency and intensity of exercise and physical activity tend to decline during pregnancy, especially among overweight and obese women.[26] Observational studies show that maternal exercise and physical activity are positively associated with better psychological well-being and reduced risk for postnatal depression.[27,28] However, results from randomized controlled trials (RCTs) on the effect of exercise training on psychological well-being diverge.[29-31]

In the Exercise Training in Pregnancy (ETIP) trial, we determined the effect of offering supervised exercise training during pregnancy on maternal and foetal outcomes among 91 women with overweight or obesity, where gestational weight gain was our primary outcome measure.[32-35] In this pre-specified[35], secondary analysis of the ETIP trial, we aimed to determine the effect of exercise training on self-perceived psychological well-being in late pregnancy and three months postpartum, and the effect of exercise training in pregnancy on the risk for postnatal depression.

Methods

Trial design

The ETIP trial was a single-centre, parallel-group RCT where we determined the effects of offering overweight and obese women supervised exercise training during pregnancy compared to standard maternal care only. The trial was undertaken at the Norwegian University of Science and Technology (NTNU) and St. Olavs hospital, Trondheim University Hospital, Norway. We started inclusion of participants in September 2010, with the last assessments in November 2015. The ETIP trial protocol and detailed description of the methods have been published elsewhere.[32,35] The study was approved by the Regional Committee for Medical and Health Research Ethics (REK-midt 2010/1522) and registered in ClinicalTrials.gov (NCT01243554). The ETIP trial was submitted to Clinical Trials September 06, 2010 with the Study Start Date set to September 2010 (Please see attached PRS Review Comments). Clinical Trials responded with a comment that they wanted us to respond to, and therefore did not release the trial immediately. Due to a delay at our Faculty's administration, the response to the comment was not submitted until November 2010.

Participants

We included women with pre-pregnancy body mass index (BMI) ≥ 28 kg/m^2, ≥ 18 year, in gestational week 12-18, and carrying a singleton live foetus at an 11–14 week ultrasound scan. Categorisation of overweight and obesity was based on the World Health Organization (WHO) classification system.[36] Pre-pregnancy BMI was self-reported. Participants had to attend assessments and exercise classes at St. Olavs hospital. Our exclusion criteria were: high risk of preterm birth, diseases that could interfere with participation, habitual exercise training at baseline (defined as exercising twice or more weekly in the period before inclusion). The women received written information and signed informed consent on behalf of themselves and their offspring before inclusion. We recruited participants through invitations sent along with notices for routine ultrasound scan appointments, information sent to general practitioners, and through Google advertisements. At the last study visit, the women received infant food worth 500 Norwegian kroner.

Intervention

All participants, regardless of group allocation, received maternity and postpartum care according to the Norwegian Standard Maternity Care for pregnant women, which is offered to all (free of charge).[37]

Women in the exercise group were offered supervised exercise sessions at St. Olavs hospital three times weekly from inclusion until delivery. The exercise program was in accordance with the recommendations from the American College of Obstetricians and Gynaecologists[25,38,39] and from the Norwegian Directorate of Health for physical activity during pregnancy.[40] The exercise sessions were supervised by a physical therapist and consisted of 35 minutes of treadmill walking at approximately 80% of maximal aerobic capacity (corresponding to Borg scale 12–15)[35] followed by 25 minutes of resistance training, including pelvic floor muscle training. In addition to the supervised program, we asked the women to exercise at home for 50 minutes at least once weekly, and to do daily pelvic floor muscle

exercises. For a full description of the exercise intervention, see previous reports (Supplementary File 1).[32,35] Adherence to the exercise program was registered in a training diary. Women in the control group were not discouraged from physical activity or exercise.

Outcomes

Sociodemographic data was collected by self-reported questionnaires at baseline assessments. Information regarding the participants' psychological well-being and risk of postnatal depression was assessed by self-reported questionnaires, completed at the hospital while they underwent a 2 h oral glucose tolerance test at baseline, late pregnancy and three months postpartum, with trial researchers available to clarify questions if needed.

Psychological well-being was assessed by the "Psychological General Well-Being Index" (PGWBI) questionnaire (PGWBI © 1984 Harold J. Dupuy, Mapi Research Trust)[41,42] at baseline (gestational week 12-18), in late pregnancy (gestational week 34-37) and three months postpartum. PGWBI measures the last week self-perceived psychological health and general well-being, and intends to assess health related quality of life or, said otherwise, to reflect a sense of well-being or distress that includes positive and negative intrapersonal affective or emotional states.[35] PGWBI consists of 22 items with six-point self-response scales that range from zero (= most negative option) to five (= most positive option). The questionnaire includes six non-overlapping dimensions: anxiety (five items), depressed mood (three items), positive well-being (four items), self-control (three items), general health (three items), and vitality (four items).[35, 38] Each dimension is summed and the total (maximum = 110) forms the overall PGWBI. The anxiety dimension assesses whether the subjects are bothered by nervousness, were generally tense, anxious, worried or upset, and/or under stress strain or pressure. Depressed-mood assesses if the participants are depressed, hopeless, or downhearted and 'blue'. Positive well-being indicates the general spirit, cheerfulness, or happiness and satisfaction with personal life. The self-control dimension intends to measure whether the subjects feel

emotionally stable, in firm control, or afraid of losing control. The general health dimension assesses if the subjects are bothered with pain, disorder, or illness and whether they are healthy enough 'to do things.' Finally, the vitality dimension contains items that assess the participants' energy, whether they feel active, vigorous, or sluggish, tired and worn out.[35]

The PGWBI questionnaire is a generic questionnaire frequently used in clinical trials across many conditions, and translated to several languages.[43-46] The PGWBI has been found suitable for subjects 14-90 years and is a highly preferred self-administered inventory.[35] The internal consistency reliability is high, with Cronbach´s alpha correlations between 0.90 and 0.94.[35] Similar correlations (Cronbach´s alpha > 0.90) have been shown for tests done in Sweden,[43] with culture and language similar to the Norwegian,[44] and recently used by Gustafsson and colleges in a clinical trial among Norwegian pregnant women.[29] The present Norwegian version of the questionnaire was translated by a standard forward-backward method at St. Olavs Hospital, the university Hospital, Trondheim, Norway, in February 2002.[47]

To measure the prevalence of symptoms of postnatal depression, the participants also completed the "Edinburgh Postnatal Depression Scale" (EPDS) questionnaire (Cox, Holden and Sagosky, 1987).[48] The EPDS questionnaire is a non-generic self-rating scale, which measures the presence of depressive symptoms during the postpartum period, indicating how the mother has felt during the last week.[48,49] The EPDS questionnaire contains 10 questions. All questions contain four response alternatives were the women are asked to "please underline the answer which comes closest to how you have felt in the past 7 days".[48] We estimated total score of the ten items using a scoring system from 0 to 3, with 0 representing the most negative option, and 3 the most positive option. Based on validations of the questionnaire,[48] we used a cut-off score of 10-12 as indication of minor depression and ≥ 13 as indication of major depression. The EPDS questionnaire is developed and commonly used for measurement of depressive symptoms in the postpartum period, but is also used and validated for the pregnancy period.[48]

The questionnaire is translated to Norwegian and valid to detect postpartum depression in a Norwegian population.[50,51]

Additionally, the participants reported their self-perceived general health status at baseline and in late pregnancy as either "very good", "good", "either good or bad", "quite bad" or "bad". This question is taken from the SF 36 Short Form Health Survey. This survey is translated to Norwegian and tested for reliability and validity in a Norwegian population.

Sample size

The sample size calculation for the ETIP trial was based on difference between groups in the primary outcome, gestational weight gain from baseline assessments to delivery (Supplemental File 1.).[32,35] Based on previous studies, a mean change of 6 kg was assumed as clinically relevant.[52,53] A two-sided, independent samples *t*-test with 5 % level of significance, standard deviation of 10, and a power of 0.90 defined our target study population of 59 in each group. We estimated the dropout rate in the trial to be 15 %, and on basis of these estimations aimed to include 150 women. We have not performed a separate power calculation for the secondary analyses reported in this paper.

Randomization and blinding

Randomisation was performed after baseline assessments using a computer random number generator, developed and administrated at the Unit for Applied Clinical Research, NTNU. The personnel who provided the participants with questionnaires regarding psychological well-being in late pregnancy and postpartum were not blinded for group allocation. Further details about randomization and blinding in the ETIP trial are published previously.[32]

Statistical methods

We confirmed baseline data normality using Shapiro-Wilk tests and visual inspection of plots and histograms. Comparisons between groups at baseline were analysed by independent samples t-tests and Fisher's Exact tests. We analysed between-groups differences in the effect of exercise training on psychological well-being (assessed by PGWBI) in late pregnancy and postpartum, and between-groups difference in "Self-perceived general health status" in late pregnancy by general linear model analysis of covariance. Changes within-groups from baseline to late pregnancy and from late pregnancy to postpartum were also analysed by general linear model analysis of covariance. Baseline values of each outcome were set as covariates in late pregnancy analyses, and late pregnancy values were set as covariates in postpartum analyses. We analysed differences between groups in EDPS using an independent samples t-test. We assessed differences in baseline PGWBI between the participants who exercised per protocol and the non-adherent participants in the exercise group by independent samples t-tests. Due to the randomisation model, we assumed no systematic differences between groups at baseline. We based our primary analyses on the "intention to treat" principle and additionally performed "per protocol" analyses, according to pre-specified cut-off values for adherence to the exercise program (Supplemental File 1.).[35] No adjustment for multiple testing have been undertaken.

We used IBM SPSS Statistics 23 and considered *P*-values < 0.05 as statistically significant.

Patient and public involvement

No patients involved.

Results

We assessed 136 women for eligibility and included 91 women, with 46 in the exercise group and 45 in the control group. Figure 1 shows the participant flow in the ETIP trial. The exercise group exercised 31.7 ± 15.3 (range 0-53) sessions at the hospital and 19.2 ± 16.5 (range 0-72) sessions at home, giving a weekly average of 1.30 ± 0.8 supervised sessions and 0.8 ± 0.7 home-based sessions. About 50% (n=19) of the women in the exercise group exercised according to our pre-specified cut-off values for per protocol analyses.

Table 1 shows the baseline characteristics of the participants. There were no statistically significant differences between the groups at baseline. Full trial baseline data have been published previously.[32] At inclusion, 55% in the exercise group and 53% in the control group reported to fulfil the recommendations for physical activity (≥ 150 min/week of moderate intensity physical activity).

In late pregnancy, 61% in the exercise group and 66% in the control group reported to adhere to the recommendations for physical activity, with corresponding numbers postpartum being 72% in the exercise group and 79% in the control group. In late pregnancy, 77% in the exercise group compared to 23% in the control group ($p < 0.01$) reported regular exercise, with corresponding numbers postpartum being 46% in the exercise group and 25% in the control group ($p = 0.16$). Approximately 58% of women in exercise group and 44% of women in the control group gained more weight during pregnancy than recommended by the Institute of Medicine (between-group difference, $p = 0.35$).[54]

Table 1. Subjects characteristics at baseline for the exercise and the control group. Observed data are presented as means ± standard deviation, or number of participants with percentages. Psychological well-being is presented with the Psychological General Well-Being Index (PGWBI) global score and six subscales.

Subjects characteristics	**Exercise Group (*n* = 46)**	**Control Group (*n* = 45)**
	Mean ± SD/N (%)	*Mean ± SD/N (%)*
Age (years)	31.3 ± 3.8	31.4 ± 4.7
Body weight (kg)	95.3 ± 12.8	98.3 ± 14.2
Body mass index (kg/m²)	33.9 ± 3.8	35.1 ± 4.6
Weight classification		
Overweight, BMI 28.0–29.9 kg/m²	3 (6.6)	5 (11.1)
Class 1 obesity, BMI 30.0–34.9 kg/m²	28 (62.2)	19 (42.2)
Class 2 obesity, BMI 35.0–39.9 kg/m²	11 (24.4)	15 (33.3)
Class 3 obesity, BMI ≥ 40.0 kg/m²	3 (6.6)	6 (13.3)
Parity		
0	22 (47.8)	19 (42.2)
1	19 (41.3)	19 (42.2)
2	5 (10.9)	4 (8.9)
≥3	0 (0.0)	3 (6.7)
Current smoking	2 (4.7)	4 (8.9)
Education		
Primary/secondary school	1 (2.3)	3 (7.0)
High school	15 (34.1)	12 (27.9)
University ≤4 years	14 (31.8)	11 (25.6)
University >4 years	14 (31.8)	17 (39.5)
Currently employed	38 (82.6)	33 (73.3)
Self-perceived general health status		
Very good	0 (0.0)	4 (9.3)
Good	25 (54.3)	19 (49.4)
Either good or bad	18 (39.1)	20 (46.5)
Quite bad	3 (6.5)	0 (0.0)
Bad	0 (0.0)	0 (0.0)
Psychological General Well-Being Index (PGWBI)	76.6±11.1	76.2±14.3
Anxiety	19.8±3.3	19.2±4.6
Depressed mood	13.2±1.9	13.2±1.9
Positive well-being	12.2±2.8	12.6±3.1
Self-Control	12.9±1.7	12.0±2.5
General Health	9.7±2.8	9.5±2.7
Vitality	8.8±3.8	10.1±3.4

Missing: Education: Control: 1. General health status: Control: 3. PGWBI: Exercise; 2, control; 4.
Statistics: Baseline variables were analysed by Independent samples t-test, and Fisher's Exact Test.

Psychological well-being in late pregnancy

We did not find any statistically significant difference between the groups in PGWBI global score, nor in any of the six subscales, in late pregnancy (Table 2). In the per-protocol analyses in late pregnancy, PGWBI global score was 80.2 (95% CI 73.9, 86.6) in participants who adhered to the exercise program in the exercise group versus 74.7 (95% CI 70.4, 79.0) in the control group (p = 0.15) (Supplementary Table 1). There were no statistically significant between-group differences in the per-protocol analyses, , but a tendency of higher "Anxiety" score in the per-protocol exercise group (21.4. 95% CI 19.7,23.2) compared to the control group (19.5, 95% CI 18.4, 20.7) (p = 0.07) (Supplementary Table 1). Figure 2 illustrates the changes in PGWBI global score and subscales from baseline to late pregnancy in each group.

Self-perceived general health status in late pregnancy was reported to be "Very good" by 9% in the exercise group and 11% in the control group, "Good" by 53% in the exercise group and 29% in the control group, "Either good or bad" by 21% in the exercise group and 50%, "Quite bad" by 15% in the exercise group and 11% in the control group, and "Bad" by 3% in the exercise group and none in the control group (between-group difference, p = 0.37). Results were similar in the per-protocol analyses (data not shown).

Psychological well-being three months postpartum

There were no statistically significant differences between the groups in PGWBI global score, nor in any of the six subscales three months postpartum (Table 2). In the postpartum per-protocol analyses, PGWBI global score among women who adhered to the exercise program in the exercise group was of 84.8 (95% CI 79.5, 90.2), versus 85.3 (95% CI 81.5, 89.2) in the

control group ($p = 0.88$), with no statistically significant differences in any of the six subscales (Supplementary Table 1). Figure 3 illustrates the changes in PGWBI global score and subscales from late pregnancy to postpartum in each group.

Table 2. Psychological general well-being (PGWBI) global score and subscales in late pregnancy and three months postpartum. "Intention to treat" model-based analyses with comparisons between groups presented as estimated mean difference with 95% confidence intervals (CI) and *p*-values.

	All participants	**Exercise**		**Control**		**Difference between groups**					
						Late pregnancy			**Postpartum**		
	Score at baseline N = 91	*Score late pregnancy N = 38*	*Score postpartum N = 36*	*Score late pregnancy N = 36*	*Score postpartum N = 34*	*Diff*	*95% CI*	*P-value*	*Diff*	*95% CI*	*P-value*
PGWBI	77.2	76.6 (72.2, 81.0)	85.4 (81.9, 88.8)	74.0 (69.4, 78.5)	84.6 (80.8, 88.4)	2.60	-3.77, 8.97	0.42	0. 77	-4.42, 5.95	0.77
Anxiety	19.7	20.7 (19.5, 22.0)	20.6 (19.5, 21.7)	19.6 (18.4, 20.8)	21.8 (20.7, 23.0)	1.12	-0.61, 2.86	0.20	-1.26	-2.98, 0.37	0.13
Depressed mood	13.4	13.2 (12.5, 13.8)	13.7 (13.2, 14.1)	13.1 (12.5, 13.8)	13.4 (12.9, 13.9)	-0.03	-0.88, 0.94	0.95	0.25	-0.43, 0.93	0.47
Positive well-being	12.5	12.0 (11.0, 13.0)	13.9 (13.0, 14.9)	12.5 (11.5, 13.5)	13.6 (12.7, 14.6)	-0.49	-1.93, 0.95	0.50	0.27	-1.07, 1.61	0.68
Self-Control	12.5	12.6 (11.7, 13.5)	13.6 (13.0, 14.1)	12.2 (11.3, 13.1)	13.1 (12.5, 13.7)	0.40	-0.87, 1.67	0.53	0.44	-0.38, 1.25	0.29
General Health	9.7	8.1 (7.1, 9.0)	11.5 (10.8, 12.2)	8.0 (7.0, 8.9)	11.2 (10.5, 11.9)	0.12	-1.24, 1.49	0.86	0.31	-0.72, 1.33	0.55
Vitality	9.5	9.8 (8.6, 11.0)	12.4 (11.3, 13.4)	9.2 (7.9, 10.4)	12.0 (10.9, 13.1)	0.65	-1.15, 2.44	0.47	0.38	-1.18, 1.94	0.63

Missing late pregnancy: Exercise 8, control, 5. *Missing postpartum:* Exercise 7, control 4.
Statistics: General linear model analysis of covariance with baseline mean and late pregnancy mean as covariates.
PGWBI = The Psychological General Well-Being Index (global score of all subscales).

Postnatal depression

We found no statistically significant difference in total EPSD score three months postpartum between the exercise group (2.96, 95% CI 1.7, 4.2) and the control group (3.48, 95% CI 2.3, 4.7) ($p = 0.55$). None reported of a total EPSD score of 13 or more, representing indication of major depression. Two women (7.1%) in the exercise group and three women (10.3%) in the control group reported at total EPSD score between 10 and 12, representing indication of a minor depression. In the per-protocol analysis, there was no statistical significant difference in total EPDS score between the exercise group (2.38, 95% CI 1.72, 4.2) and the control group (3.48, 95% CI 2.3, 4.7) ($p = 0.30$).

Baseline comparison within the exercise group

Women in the exercise group who adhered to the intervention protocol reported a higher "Self-Control" subscale score at baseline (13.5 vs 12.4, $p = 0.04$) and a tendency of higher "Depressed mood score" (13.8 vs 12.8, $p = 0.07$), compared the non-adherent women in the exercise group.

Harms

We did not register any adverse events related to the intervention program or the assessments in the ETIP trial. One woman in the control group reported a score indicating suicidal risk (EDPS). This participant got an immediate appointment with her general practitioner.

Discussion

Main findings

We found no statistically significant effects of offering supervised exercise training during pregnancy on psychological well-being in late pregnancy or three months postpartum, nor on symptoms of postnatal depression, among women who are overweight or obese. Both the exercise group and the control group reported of good psychological well-being during pregnancy and postpartum and both groups had a low of risk for postnatal depression. The psychological well-being was stable during pregnancy and increased significantly from late pregnancy to postpartum in both groups. The women in the exercise group who adhered to the exercise protocol were characterized by higher self-control and fewer symptoms of depression at baseline, compared to the non-adherent women in the exercise group. Only 50% of the women in the exercise group followed the exercise-protocol and we included less participants than estimated in the trial protocol.

Strengths and weaknesses of the study

The major strength of this study was the randomised controlled design. We assessed well-being by valid and reliable questionnaires.[55,56] We included only women with pre-pregnancy overweight and obesity (BMI $\geq$ 28 kg/m^2) in the trial, contributing to a homogenous study group. We recorded exercise adherence as well as self-reported physical activity levels throughout the trial period in both groups.

Limitations of the ETIP trial include a limited study sample, 20% dropout, and only 50% adherence to the exercise protocol.[32] The low adherence to the exercise protocol may be explained by discomfort (especially in the first trimester), by the women being anxious about getting exhausted, by having trouble with prioritizing time for exercise, and by lack of motivation for lifestyle changes.

These factors limit the chance of estimating a true effect of exercise training on psychological well-being. Furthermore, the relatively high level of physical activity in the control group could have reduced the chance of finding an effect of the intervention. Our trial included comprehensive health assessments and close monitoring of the women, regardless of group allocation. This close follow-up by health personnel may have prevented reduced psychological well-being among all the women in the trial. We had no information on previous mental health history or use of antidepressant treatment among the participants.

Comparison with other trials

Observational studies show that women who are physically active during pregnancy report better psychological well-being than less active women[28] and that the risk of psychological health problems increases in parallel to decreased frequency of exercise during pregnancy.[27] A limited number of RCTs have investigated the effects of exercise training in pregnancy on psychological well-being, and the results diverge.[29,30,57] Bogaerts and colleagues[30] showed reduced anxiety in late pregnancy among obese women who received an intervention combining regular motivational interviewing with advice about healthy eating and physical activity in pregnancy, compared to advice only or a standard care control group. They found no effect of the intervention on depression.[30] In our study, the level of anxiety did not differ between groups in late pregnancy, but we observed a tendency of less symptoms of anxiety among the women who adhered to the exercise program compared to the control group, which indicates a positive effect of regular exercise during pregnancy on the risk of anxiety. Gustafsson and co-workers[29] investigated the effect of regular exercise during pregnancy on late pregnancy psychological well-being using PGWBI. They included women in all BMI categories, and found, similar to our trial, no effect of exercise on mental health. Also in their trial, the participants reported of good psychological well-being at baseline. This is in contrast to previous studies showing a high prevalence (15-25%) of depression and anxiety among

overweight and obese pregnant women[2,7,8,58-61] and that especially the levels of anxiety increases from early to late pregnancy in this population.[59] Compared to the general population of pregnant women with overweight/obesity, a higher percentage of women in the ETIP trial reported to fulfil the recommendations for physical activity during and after pregnancy[32], the number of pregnancy complications were lower, as was the percentage of women exceeding the Institute of Medicine guidelines for gestational weight gain.[32,33] Low level of physical activity and exceeding the recommended gestational weight gain are both associated with increased risk for reduced psychological well-being, and these factors could therefore explain stabile PGWBI scores during pregnancy in our study group. Again, this indicates that we included women with good psychological well-being in our trial.

We found no effect of exercise training on the risk for postnatal depression, which is in line with previous studies suggesting limited effect of exercise interventions during pregnancy on risk for depression after delivery.[31,57] Few of the participating women reported symptoms of postnatal depression in our trial. This is in contrast to a systematic review and meta-analysis reporting a high risk of developing depression during the postpartum period for women with pre-pregnancy obesity.[1] Also a cohort study by Ertel and collegues,[5] who assessed postnatal depression among 1686 women in all BMI categories, found that pre-pregnancy BMI >30 was associated with increased risk for depression six months postpartum. The EDPS records the woman's self-perceived psychological well-being during the last week, and thereby the woman's current state of anxiety and depression. On the other hand, the "State and Trait Anxiety Inventory (STAI)" questionnaire, assesses both short-term and long-term symptoms, and might provide a different set of information compared to the EDPS. Even though the EDPS is the most frequently used questionnaire for assessing risk for depression postpartum, the use of different questionnaires in comparative trials hampers comparison between studies.

Generalizability and clinical implications

When compared to women in the Norwegian Medical Birth Registry,[62] the ETIP participants are representative for Norwegian pregnant women with overweight/obesity, according to BMI, obesity grades I, II, III, age, education, parity and occupational activity/employment.[32] However, it is likely that women who volunteer for participation in an exercise trial are extra aware of possible benefits of maternal exercise, are more experienced with physical activity and suffer from less pregnancy complications. We believe that the findings of our study can be generalized to relatively healthy pregnant women with pre-pregnancy BMI of 28 or more.

We based the trial intervention program on current recommendations for maternal exercise and designed it for easy implementation into clinical practice. Health care professionals, especially general practitioners and midwifes who consult pregnant women, are in a unique position to inform, help and guide women with high BMI throughout pregnancy. Distinct recommendations for exercise and physical activity should be given to all pregnant women, and the women should be closely monitored and motivated by maternal health care personnel throughout pregnancy. Assessing psychological well-being early in pregnancy may be important for prediction of adherence to exercise during pregnancy.

Conclusion

We found no statistically significant effects of supervised exercise training during pregnancy on psychological well-being in late pregnancy or postpartum, nor on the prevalence of symptoms of postnatal depression, among women with overweight or obesity. Both the exercise group and the control group reported good psychological well-being and low risk for postnatal depression. The level of self-control early in pregnancy may be important for exercise adherence during pregnancy. Low adherence to the exercise protocol in our trial could have reduced the chance of finding an effect of regular maternal exercise on mental health.

We need adequately powered trials, with good adherence to the intervention protocol, to be able to investigate the true effect of exercise during pregnancy on maternal well-being and to examine factors associated with motivation for exercise during pregnancy.

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Author Contributions: KKG acquired the data, analysed the data, interpreted the data and drafted the manuscript. ASH interpreted the data and critically revised the manuscript. SM designed the study and critically revised the manuscript, SNS designed the study and critically revised the manuscript, KÅS designed the study and critically revised the manuscript, ØS provided the statistics in previous published papers in the ETIP trial, and reviewed statistical methods in the current manuscript, TM acquired some of the data, deigned the study and critically revised the manuscript. All authors have approved the final version of the manuscript and are accountable for all aspects of the work.

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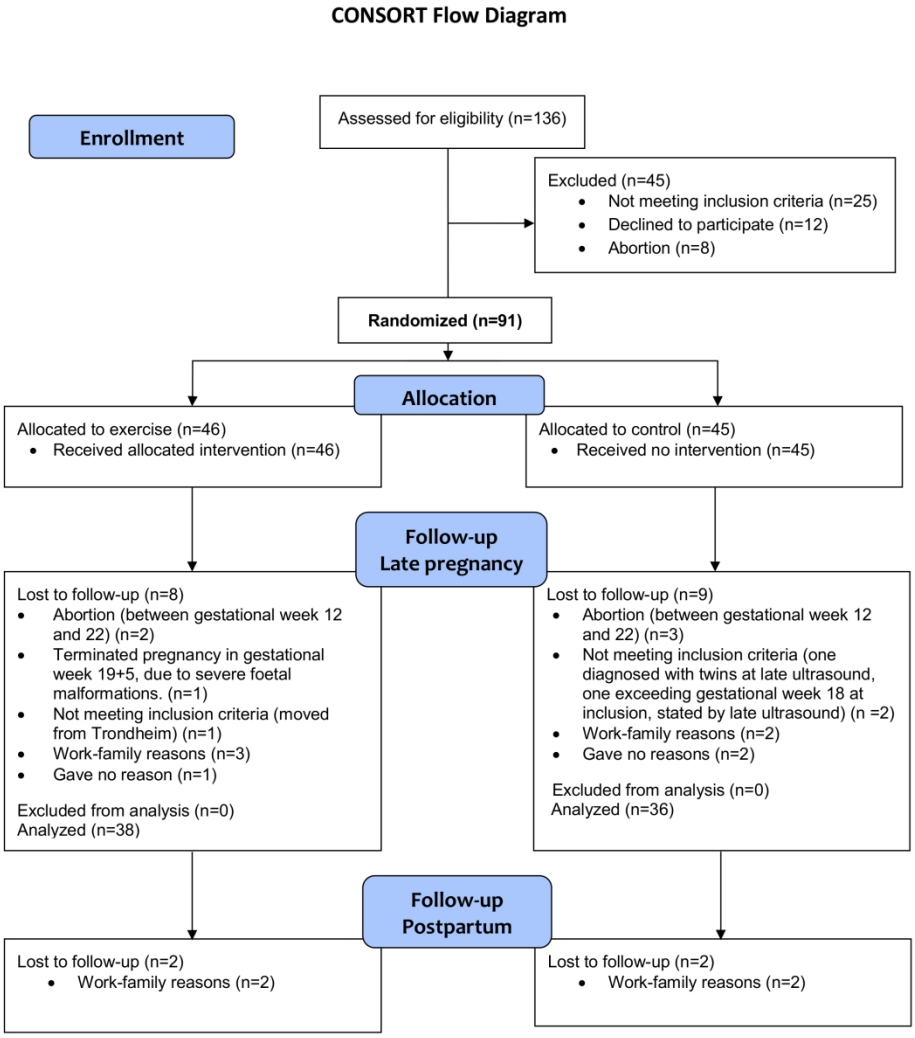
Figure legends

Figure 1. CONSORT flow chart ETIP trial.

Figure 2. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from baseline to late pregnancy in the exercise group and the control group. Data are means with 95% confidence intervals.

Figure 3. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from late pregnancy to postpartum in the exercise group and the control group. Data are means with 95% confidence intervals.



CONSORT Flow chart ETIP trial

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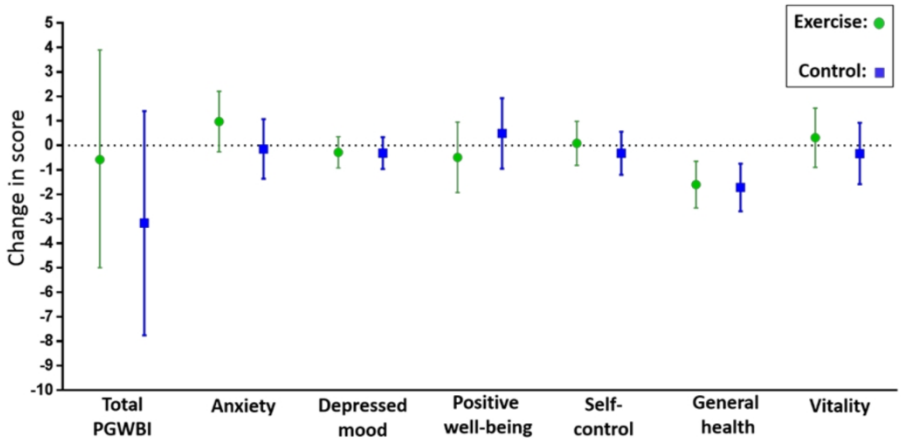

Figure 2. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from baseline to late pregnancy in the exercise group and the control group. Data are means with 95% confidence intervals.

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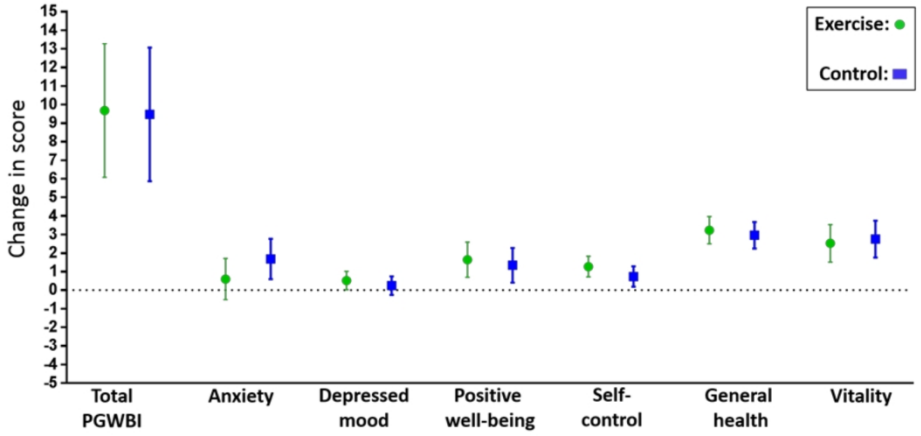

Figure 3. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from late pregnancy to postpartum in the exercise group and the control group. Data are means with 95% confidence intervals.

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Supplementary Table 1. Outcomes in PGWBI at late pregnancy and three months postpartum. "Per-protocol" model based analyses with comparison between groups presented as estimated mean difference, 95% confidence interval (CI) and *p*-value.

	Exercise Per protocol		**Control**		**Difference between groups**					
					Late pregnancy			**Postpartum**		
	Score late pregnancy N = 19	*Score postpartum N = 19*	*Score late pregnancy N = 36*	*Score postpartum N = 34*	*Diff*	*95% CI*	*P-value*	*Diff*	*95% CI*	*P-value*
Anxiety	21.4 (19.7, 23.2)	20.9 (19.3, 22.4)	19.5 (18.4, 20.7)	21.7 (20.7, 22.7)	1.88	-0.17, 3.93	0.07	-0.80	-2.66, 1.07	0.39
Depressed mood	13.6 (12.4, 14.3)	13.6 (12.8, 14.4)	13.2 (12.5, 13.8)	13.5 (12.9, 14.1)	0.20	-0.93, 1.33	0.72	0.14	-0.82, 1.10	0.77
Positive well-being	12.3 (11.0, 13.7)	14.2 (12.8, 15.6)	12.8 (11.9, 13.7)	13.9 (12.9, 14.8)	-0.41	-2.02, 1.24	0.62	0.36	-1.31, 2.03	0.66
Self-Control	13.2 (11.8, 14.6)	13.3 (12.4, 14.3)	12.1 (11.2, 13.0)	13.1 (12.5, 13.7)	1.05	-0.63, 2.73	0.21	0.18	-0.96, 1.32	0.75
General Health	8.5 (7.0, 10.0)	11.6 (10.4, 12.8)	8.1 (7.1, 9.1)	11.3 (10.5, 12.1)	0.45	-1.35, 2.25	0.62	0.31	-1.15, 1.76	0.67
Vitality	10.9 (9.0, 12.7)	12.0 (10.4, 13.6)	9.6 (8.4, 10.8)	12.3 (11.2, 13.4)	1.28	-0.96, 3.52	0.26	-0.29	-2.31, 1.74	0.77
PGWBI Index	80.2 (73.9, 86.6)	84.8 (79.5, 90.2)	74.7 (70.4, 79.0)	85.3 (81.5, 89.2)	5.55	-2.13, 13.2	0.15	-0.49	-7.18, 6.20	0.88

Missing late pregnancy: Exercise 6, control, 5. *Missing postpartum:* Exercise 5, control 4.
Statistics: General linear model analysis of covariance, with baseline mean as covariate in late pregnancy analyses, and late pregnancy mean as covariate in the postpartum analyses.
PGWBI: The Psychological General Well-Being Index (global score of all subscales).

Moholdt et al. Trials 2011, 12:154
http://www.trialsjournal.com/content/12/1/154

TRIALS

STUDY PROTOCOL Open Access

Exercise Training in Pregnancy for obese women (ETIP): study protocol for a randomised controlled trial

Trine T Moholdt[1,3*], Kjell Salvesen[2], Charlotte B Ingul[3], Torstein Vik[4], Emily Oken[5] and Siv Mørkved[1]

Background: Both maternal pre-pregnancy obesity and excessive gestational weight gain are increasing in prevalence and associated with a number of adverse pregnancy outcomes for both mother and child. Observational studies regarding physical activity in pregnancy have found reduced weight gain in active mothers, as well as reduced risk of adverse pregnancy outcomes. There is however a lack of high quality, randomized controlled trials on the effects of regular exercise training in pregnancy, especially those with a pre-pregnancy body mass index (BMI) at or above 30 kg/m^2.

Methods: We are conducting a randomised, controlled trial in Norway with two parallel arms; one intervention group and one control group. We will enroll 150 previously sedentary, pregnant women with a pre-pregnancy BMI at or above 30 kg/m^2. The intervention group will meet for organized exercise training three times per week, starting in gestation week 14 (range 12-16). The control group will get standard antenatal care. The main outcome measure will be weight gain from baseline to delivery. Among the secondary outcome measures are changes in exercise capacity, endothelial function, physical activity level, body composition, serum markers of cardiovascular risk, incontinence, lumbopelvic pain and cardiac function from baseline to gestation week 37 (range 36-38). Offspring outcome measures include anthropometric variables at birth, Apgar score, as well as serum markers of inflammation and metabolism in cord blood.

Discussion: The results of this trial will provide knowledge about effects of regular exercise training in previously sedentary, obese pregnant women. If the program proves effective in reducing gestational weight gain and adverse pregnancy outcomes, such programs should be considered as part of routine pregnancy care for obese women.

Trial Registration: ClinicalTrials.gov: NCT01243554

Background

In the Unites States over one-third of reproductive age women are obese (body mass index (BMI) ≥ 30 kg/m^2) and another 29% are overweight (BMI 25.0-29.9 kg/m^2) [1]. Maternal obesity is associated with a number of adverse outcomes during and after pregnancy, such as gestational diabetes, preeclampsia, caesarean delivery and children born large for gestational age [2], as well as increased risk for childhood obesity among offspring. In addition, over 60% of overweight women gain more than recommended during pregnancy [3]. As gestational weight gain is directly associated with maternal weight retained during the postpartum period [3] as well as with offspring adiposity in childhood [4] and in early adulthood [5], excess gestational weight gain could accelerate the obesity epidemic. Current recommendations say that pregnant women should exercise with moderate intensity for 30 minutes or more on most, if not all, days of the week [6]. In general, women are not active enough during pregnancy and women who have a high pre-pregnancy BMI are even less likely to be physically active [7].

Today's knowledge about the importance of exercising regularly in controlling weight gain in pregnancy is

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mainly based on results from observational studies [4,8-11]. Previous randomized controlled trials of physical activity during pregnancy are few in number and have had varying results. For example, Clapp et al [12] found significantly less weight gain in women who were randomized to high volume of exercise in late pregnancy, compared to moderate or low volumes, whereas others have found no significant effects of exercise training on gestational weight gain [13-15]. The reasons for the divergent results in these randomized trials could be low compliance, high drop out rates and inadequate number of participants in some of the studies, as well as differences in the mode, frequency, intensity and duration of the exercise training. A reduced risk of excessive weight gain has been found in women randomized to lifestyle counselling programs combining diet and exercise [16,17]. In such programs however, it is hard to say if it is the exercise component or other factors that make the women gain less weight in the intervention groups. Thus, there is a lack of good quality randomized controlled trials, assessing short and long term effects of physical activity in pregnancy on mothers and offspring. Especially, there is a need for studies looking at potential effects of regular exercise training during pregnancy in obese mothers.

In this paper, we describe the methods of the Exercise Training in Pregnancy (ETIP) trial, a randomized, controlled trial of physical activity during pregnancy.

Methods

Objectives

The primary objective of the ETIP trial is to test the hypothesis that obese pregnant women who exercise in addition to usual pregnancy care will have a lower gestational weight gain compared to women who receive usual care only.

Secondary, the ETIP trial will investigate the effects of exercise training on various pregnancy-related complications, such as insulin resistance, lumbopelvic pain, urinary and fecal incontinence, pelvic floor muscle dysfunction, and prolonged labour. We will also assess possible effects of exercise training on cardiopulmonary parameters as cardiac function, submaximal oxygen uptake, lactate threshold, heart rate recovery, endothelial function, and blood pressure, measured as changes in these parameters from early to late pregnancy. Offspring variables include Apgar score, weight, length and head circumference at delivery, prevalence of large for gestational age (LGA) and small for gestational age (SGA), blood pressure, and body composition, and cord blood markers of inflammation and insulin resistance.

Our hypothesis is that regular exercise training in pregnancy will reduce gestational weight gain and pregnancy-related complications. We also hypothesise that exercise will increase physical capacity, heart rate recovery and endothelial function, and reduce blood pressure, compared to the control group. Regarding offspring variables, we hypothesise that exercise training will reduce the prevalence of LGA, blood pressure, cord blood markers of inflammation and insulin resistance, as well as improve body composition, and Apgar score.

Participants and setting

We invite pregnant women with self-reported pre-pregnancy BMI ≥ 30 kg/m^2 to participate in the trial. Women are eligible if they are 18 years or older, with a singleton live fetus at an 11-14 weeks ultrasound scan. Exclusion criteria are pregnancy complications, high risk for preterm labour or diseases that could interfere with participation, and habitual exercise training (twice or more weekly). The women are given information about the project and will be recruited through the ordinary visits at general practitioners and midwives, and at outpatient clinics at the hospitals. Also, information about the study and invitation to participate is sent along with the invitation to come for routine ultra sound scan in week 18.

The trial will be conducted at the Norwegian University of Science and Technology and the St.Olavs Hospital, Trondheim University Hospital. The recruitment started in September 2010 and will continue until the needed number of participants is included, anticipated until the end of 2012. Participating women get infant food worth $85 US dollars.

Randomisation and allocation

After initial assessments, the women will be randomly assigned to either intervention or control (1:1 randomisation, Figure 1). Allocation is performed by a web-based randomisation system developed and administered by another unit at the university to ensure blinding. The randomisation will be in blocks with varying block size.

Intervention

We invite the training group to participate in an exercise program that we have specially designed for pregnancy, including aerobic activity, specific exercises for stabilization of the lower back and pelvis, and strength exercises for the pelvic floor muscles that we have specially designed for pregnancy. We conduct training groups for a total of 60 minutes four times weekly at the hospital. We ask the women to come to exercise training a minimum of twice weekly between 14 and 37 weeks of gestation. We also encourage the women to come for exercise training even after week 37. The endurance training consists of a 10 minute warm-up followed by walking on treadmills for 25 minutes. The intensity will be moderate, reaching ~80% of their

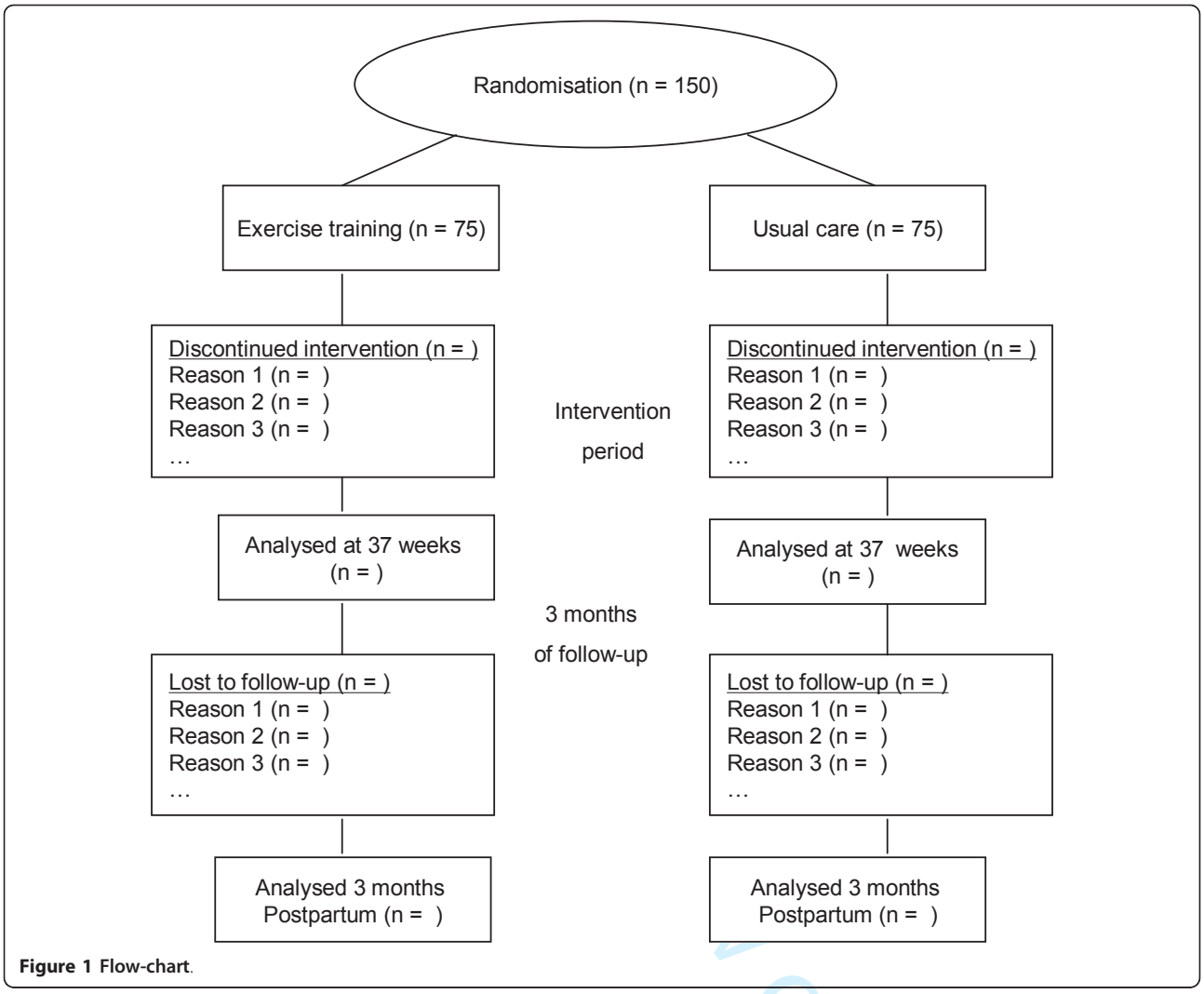

Figure 1 Flow-chart.

maximal capacity in periods (corresponding to Borg scale12-15) [18].

In addition, we instruct intervention women in a 50 minute home exercise program which we encourage them to complete at least once per week (35 minutes endurance training and 15 minutes strength exercises). We also teach pelvic floor muscle exercises to do daily. We also recommend the women to be physically active in every-day life. Adherence is strongly emphasized and registered in the women's personal training diary and the reports from the persons leading the training groups. During the training period, the subjects will go through motivational interviewing [19]. This is a client-centred therapeutic method to enhance readiness for change and to elicit the client's own motivations for change. Each woman will go through a 30 minute session of motivational interviewing in each trimester. They will also receive a weight gain curve that shows the recommended weight gain throughout pregnancy, based on 2009 Institute of Medicine guidelines [20]. The training protocol follows recommendations from the Norwegian Health Directory [21] and the American College of Obstetrics and Gynecology [6]. Specific adjustments are made to the exercise program if needed (for example by using a stationary bike instead of treadmill walking and by modifying the strength exercises to the actual strength level of the participants).

Women in the control group will receive the customary regular consultations with midwife, general practitioner or obstetrician. They are not discouraged from exercising on their own. Neither group will receive special recommendations about diet, beyond what is given through standard antenatal care. In Norway, the pregnancy care is free of charge. Routine prenatal visits are done by general practitioners, midwives, or a combination of the two, and are usually undertaken in gestational weeks 8-12, 24, 28, 32, 36, 38, 40, and 41. In addition, women are invited to an ultrasound scan is

gestational week 18. There is currently no knowledge about the actual advices about physical activity that prenatal care providers give to pregnant women, but the guidelines from the Norwegian Health Directory [21] are in line with the international guidelines [6].

Study assessment visits

We will see women for research visits at baseline (12-16 weeks of pregnancy), and again in week 37 (range 36-38), as well at three months post partum (Figure 2). We also obtain clinical measures that are collected during the delivery hospitalization as well as through primary care.

Primary outcome measure

The primary outcome measure is gestational weight gain, calculated as the difference between weight measured at the time of inclusion and weight just before delivery. We measure maternal body weight at enrolment and before delivery to the nearest 0.1 kg with a calibrated electronic scale (SECA 770, Medema, Norway) with participants wearing indoor clothing, without shoes. Hospital staff will measure weight during the delivery hospitalization using a different scale than at baseline. We will calibrate the scales to ensure comparability. If the hospital staff forget to weight the women, we will use their self-reported weight at the time of delivery as the outcome measure.

Secondary outcome measures

The maternal secondary outcome measurements are outlined in Figure 2 and described more in detail below.

Blood sampling for fasting glucose concentrations and the other blood markers will be taken after a 10 hour overnight fast, and glucose tolerance will be measured by a 2 hour 75 mg per-oral glucose tolerance test. Gestational diabetes is diagnosed as fasting glucose ≥ 6.9 mmol/L or 2 h concentration ≥ 7.8 mmol/L [22]. Insulin resistance will be calculated using the homeostasis model assessment (HOMA-IR). We will analyse fasting blood for concentrations of lipids, ferritin, haemoglobin, high-sensitive C-reactive protein, and insulin c-peptide. We will also collect whole blood and serum to be frozen at -80C and stored in a biobank for

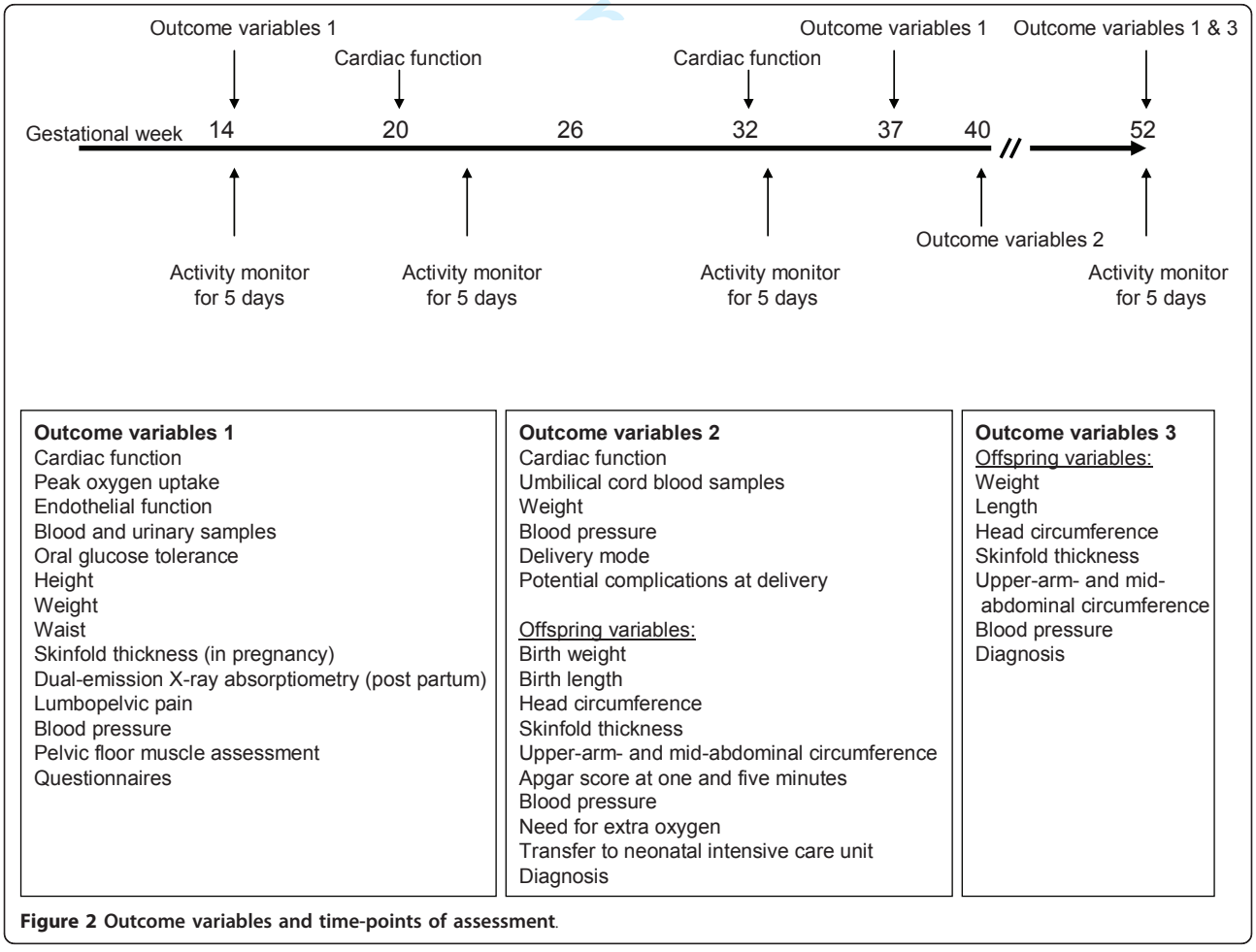

Figure 2 Outcome variables and time-points of assessment.

later analyses of hormones associated with female reproduction and blood markers associated with adiposity and insulin resistance. We will also collect Tempus blood RNA tubes and urinarysamples to be frozen for later analyses.

Body height will be measured by a wall mounted height scale. Body composition will be assessed by skinfold thickness during pregnancy and also by dual energy x-ray absorptiometry (DEXA-scan) at three months postpartum. Skinfold thickness will be measured at the right side of the body at the following sites: triceps, biceps, and subscapular, by Harpenden Caliper (Holtain Ltd, UK). Sum of skinfold thickness are measured and used for later calculation of body fat percentage. Waist circumference is measured at all time points at the level of the umbilicus. DEXA (Hologic Discovery-A: Integrity Medical Systems) will be used to measure body composition after 10 hours of fasting, to decrease large variations in hydration status (postpartum only).

Lumbopelvic pain (Disability Rating Index) and physical examination of lumbar spine and pelvic region are done by experienced physical therapists. Tests used are active straight leg raising [23] and the posterior pelvic pain provocation test [24].

Prevalence and severity of urinary- and fecal incontinence will be assessed by questionnaires [25,26], muscle strength measurements, 2D and 3D ultrasound investigation of the pelvic muscles, and clinical examination and palpation of the pelvic floor muscles. Pelvic floor muscle strength, and vaginal squeeze pressure, will be measured using a vaginal balloon catheter with a balloon size of 6.7 × 1.7 cm connected to a pressure transducer [27].

Psychological well-being and postnatal depression will be assessed using standardized questionnaires (The Psychological General Well-Being inventory [28] and The Edinburgh Postnatal Depression Scale [29], respectively). Also, the women will fill in a questionnaire about delivery expectancy (The Wijma Delivery Expectancy/Experience Questionnaire [30]) Quality of life will be assessed by the generic SF-8 Quality of life questionnaire [31]. To register diet during the intervention period, the women will fill in a validated Norwegian quantitative food frequency questionnaire [32].

Prevalence of pre-eclampsia will be registered by use of the women's health certificates. We will measure systolic and diastolic blood pressure with an automatic device, after 15 minutes of supine resting and use the average of three repeated measurements taken with two minutes intervals. We will measure endothelial function by flow-mediated dilatation of the brachial artery using ultrasound (Vivid 7, GE Vingmed Ultrasound, Norway). The women will fast and abstain from exercise, caffeine, and smoking for ten hours, and rest for 10 minutes before the measurements. The recordings are done 5 cm above the antecubital fossa before inflation of a pneumatic cuff on the lower arm for 250 mm Hg for five minutes, and again directly after cuff release and for five minutes. The responses will be analysed by a automatic detection program, and will be reported both as absolute changes and as responses normalized by dividing the percentage change in diameter by the shear rate.

Physical activity will be registered by questionnaires. Both groups will also wear a activity monitor (Sensewear Armband, APC Cardiovascular, UK) to register their level of daily physical activity for one week in early (before week 17), mid (week 19-24) and late (after week 28) pregnancy. This armband includes a two-axis accelerometer, a heat flux sensor, a galvanic skin response sensor, a skin temperature sensor and a near-body ambient temperature sensor, and has been validated during pregnancy (Berntsen et al, In review/in press Acta Obstetrica et Gyencologia Scandinavia). In addition, the training group will fill in a training diary.

Maternal cardiac function will be measured using echocardiography. The assessments will be done at week 14, week 20, and week 32, as well as 48 hours after delivery, and again at three months post partum (Figure 2). A full resting echocardiogram will be performed with a Vivid 7 scanner (GE Vingmed Ultrasound, Horten, Norway) using a phased-array transducer. Three cine loops from the three standard LV apical planes (four-chamber, two-chamber and long-axis), right ventricle and LV parasternal view will be recorded in B- mode and tissue Doppler mode simultaneously. Conventional Doppler flow parameters will be measured as well as tissue Doppler imaging with pulsed tissue Doppler in the AV-plane and strain/strain rate of the 16 segments of the left ventricle (with tissue Doppler and speckle tracking). For automated identification of myocardial segments and analysis, we will use a customized post-processing system (GcMat, GE-Vingmed, Horten, Norway).

Multistage submaximal exercise tests will be done on treadmills. After familiarizing with walking on a treadmill and 2-3 minutes of warming up, the test begins with walking at 4,5 km/h and 0% inclination. Each stage is 4 minutes and the inclination is elevated 3% each stage. Heart rate and oxygen uptake will be measured continuously during the test. Blood lactate, blood pressure and perceived exertion (according to the Borg 6-20 scale, [18]) will be recorded at the end of each stage. Tests are terminated if the subjects are feeling unwell (have symptoms of pain, nausea, or dizziness), if the heart rate exceeds 185 beats per minute, or if systolic and diastolic blood pressure exceeds 200 and 100 mmHg, respectively.

At delivery, we register mode of delivery and potential complications. Offspring variables include are outlined in Figure 2, and include the child's condition at birth and in the newborn period, birth weight, birth length, head circumference, subscapular and triceps skinfold thickness, upper-arm- and mid-abdominal circumferences, cord blood markers of inflammation and insulin resistance, and blood pressure. The child's condition include Apgar scores at one and five minutes as recorded by the attending mid-wife or physician, birth traumas, need for extra oxygen, transfer to neonatal intensive care unit, and diagnosis. The anthropometric measurements will be standardized according to Vik et al [33].

We intend to follow the children at age 3 and 12 months. At these time points we will also register breast feeding and the use of supplementary feeding, as well as crying behaviour according to Wessel et al [34]. Neuromotor development will be recorded through milestones, and by using the age and stages questionnaire at 12 months of age [35]. This instrument has been validated in Norway [36]. We also intend to follow these children for a longer time in order to study possible long term effects of in utero exposure to maternal exercise training.

Sample size

Based on prior studies [37,38], the power calculation has taken into account a 6 kg expected and clinically relevant difference between mean weight increases in the control group compared to the training group (between baseline and delivery). Based on this assumption, an independent samples t-test, 5% level of significance and test strength of 0.90, gives a study population of 59 in each group. A 15% estimated drop-out requires a total of 150 included obese pregnant women, 75 enrolled in each arm.

Ethical considerations

The Regional Committee for Medical Research Ethics has approved the study, and it will be conducted in accordance with the Declaration of Helsinki. All mothers will give their informed, written consent to participate.

Blinding

Baseline measurements, except for the armband registration of physical activity, will be done before randomisation. Later assessments will be done both blinded (echocardiography, pelvic floor assessments, blood analyses, all offspring variables) and non-blinded to group allocation (weight, skinfold measurements, lumbopelvic pain, oxygen uptake and endothelial function recordings). Although endothelial function recordings are done non-blinded, the analyses of these data will be done blinded to both group allocation and time of measurement.

Statistical methods

The principal analysis will be done on an intention-to-treat basis; outcome measures will be analyzed according to the treatment arm to which patients are randomized regardless of subsequent crossover or non-adherence. To model the outcome variables over time, we will use a linear mixed effects model [39]. Age, parity, and BMI will be considered as potential covariates to improve precision. We will also do post-hoc comparisons of time points within groups, looking at within-group changes in outcome variables from gestational week 14 to 37, as well as from gestational week 37 to 12 weeks post partum.

In addition to the primary analysis, we will split the women according to if they have actually been exercising during pregnancy or not. The cut-off for this analysis will be: 1) attending ≥ 42 organised exercise sessions, or 2) attending ≥ 28 exercise sessions + performing ≥ 28 home exercise sessions, or 3) performing ≥ 60 home exercise sessions. To count as a home exercise session, the exercise should be ≥ 50 minutes (either aerobic or strength training) of at least moderate intensity. We also intend to compare women fulfilling the general recommendations for healthy adults of exercising moderately for 30 minutes daily [40], with the ones below this threshold. Results will be given as mean values with 95% confidence intervals. P-values < 0.05 will be considered significant.

Discussion

Maternal obesity is regarded a high-risk obstetric condition and is associated with pregnancy complications and adverse outcomes [2]. In addition, there is increasing evidence that gestational weight gain may be an important predictor of the women's risk of subsequent obesity and diabetes. It has therefore been proposed that pregnancy is a unique period of time with regard to changing women's behaviour [41]. In the present study, we aim to prevent excess gestational weight gain and obesity related pregnancy complications through regular exercise training throughout pregnancy.

A recent study showed that approximately 60% of overweight women gain more than recommended during pregnancy, and as gestational weight gain associates with weight retained during the postpartum period [3], excess gestational weight gain could accelerate the obesity epidemic. Thus the prevention of weight gain in overweight and obese pregnant women is an important public health issue. Further, maternal obesity is associated with a number of adverse outcomes during and

after pregnancy, such as gestational diabetes, preeclampsia, caesarean delivery and children large for gestational age [2]. The risk for gestational diabetes is increased 2-3 fold with obesity, and fetuses of obese mothers have higher risk of developing insulin resistance in utero [42]. Greater maternal gestational weight gain has also repeatedly been found to associate with offspring adiposity in childhood [4] and in early adulthood [5]. As obese children have elevated levels of inflammatory markers related to cardiac disease manifested later in life [43], they will be at increased risk for subsequent cardiovascular disease. Importantly, there are indications in the recent literature that the prenatal environment plays a role for children obesity, independent of genetic predisposition and shared eating habits [44,45].

Strengths of our study include the thorough testing that will be done of the women as well as their offspring; investigating possible effects of exercise training on weight gain, endothelial function, insulin resistance, cardiac function, incontinence problems, lumbopelvic pain, and psychological wellbeing. In addition we collect comprehensive information on physical activity, using both subjective and objective measurements (questionnaire and armband activity registrations, respectively), as well as on dietary habits. Also regarded as a strength of the study, is the composition of the exercise training program, comprising both endurance training, general strength training and specific pelvic floor exercises.

A possible weakness of our study is that it could be underpowered for small differences in gestational weight gain between groups. Also, we think that women who like to participate in this kind of study are motivated for exercise and thereby that some of the women in the control group will do regular exercise training on their own. Such cross-over from the control group would potentially lead to smaller between-group differences.

The results from our study will give grounds for giving advice as well as organizing exercise training groups for women with obesity entering pregnancy. If women randomized to training manage to reduce their gestational weight gain compared to controls, such programs should be considered as part of the regular pregnancy care for this high-risk obstetric group.

In addition to effects on weight gain, we hope to see a reduction in other pregnancy complications. Our study will investigate the ability of regular exercise training to prevent gestational diabetes mellitus, as well as the effect on serum biomarkers associated with insulin resistance and inflammation. Previous work have found that exercise training may reduce lumbopelvic pain [46,47], however, a preventive effect of exercise during pregnancy remains unclear. Pregnancy and childbirth may also cause urinary and fecal incontinence, and obesity is an additional risk factor. The average prevalence of urinary incontinence during pregnancy and after delivery is 30-40%, and of fecal incontinence after delivery 4-5% [48]. Specific pelvic floor muscle exercises in pregnancy and post partum reduce urinary incontinence, while the preventive effect on fecal incontinence is less documented [49].

Although observational evidence is quite consistent regarding the association between large gestational weight gain and offspring adiposity, the evidence for causality is still lacking. It is possible that the intrauterine experience of infants born to mothers who gain a lot when pregnant programs long-term weight regulation, or the maternal weight gain could just be a marker of other, shared causes of both maternal and offspring weight [50]. The optimal way to explore the impact of the intrauterine exposure upon child adiposity, would be to randomized women to usual care or to an effective intervention limiting gestational weight gain, and then to follow the infants longitudinally. To our knowledge, no such adequately powered, randomized trial has been done to investigate the possible causality between excess gestational weight gain and child obesity. The randomized trial we propose here will provide evidence for such a causal relationship.

List of abbreviations

ETIP: Exercise training in pregnancy; BMI: Body mass index; LGA: Large for gestational age; SGA: Small for gestational age; HOMA-IR: Insulin resistance homeostasis model assessment; DEXA: dual energy x-ray absorptiometry; 2D: two-dimensional; 3D: three-dimensional; SF-8: Short form 8; LV: left ventricular; AV-plane: atrioventricular plane

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Authors' contributions

TMparticipated in the design of the study, coordinates the study and drafted the manuscript. KÅS participated in conceiving and designing the study and in critically revising the manuscript, as well as approving the final version to be published. CBIparticipated in conceiving and designing the study and in critically revising the manuscript, as well as approving the final version to be published. TVparticipated in conceiving and designing the study and in critically revising the manuscript, as well as approving the final version to be published. EOparticipated in conceiving and designing the study and in critically revising the manuscript, as well as approving the final version to be published. SMparticipated in conceiving and designing the study and in

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Competing interests
The authors declare that they have no competing interests.

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	5
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6-7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	5
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7-8
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7-8
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7-8
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7-8
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	7-8

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	9
	13b	For each group, losses and exclusions after randomisation, together with reasons	9
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9
	14b	Why the trial ended or was stopped	5
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	10
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	10, 12
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	11, 12, 13
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	11, 12, 13
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	13
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	14, 15
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	16, 17
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	17
Other information			
Registration	23	Registration number and name of trial registry	3
Protocol	24	Where the full trial protocol can be accessed, if available	18
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.