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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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Manuscripts

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3 **Effects of supervised exercise training during pregnancy on psychological well-being**
4 **among overweight and obese women. Secondary analyses of the ETIP-trial, a randomized**
5 **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/m².

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

Setting: University Hospital, Norway

Participants: Ninety-one women (age 31.2 \pm 4.1 years, BMI 34.5 \pm 4.2 kg/m²) 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 \pm 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

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3 depression. The study participants reported good psychological well-being and had a low risk
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5 for postnatal depression.
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11 **Trial registration number:** ClinicalTrials.gov NCT01243554
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14 **Key words:** Maternal health, mental health, depression, anxiety, pregnancy complications
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17 18 19 20 21 **Article summary** 22

23 24 25 **Strengths and limitations of this study:** 26

- 27
28 • Randomized controlled trial
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30 • Supervised exercise program
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32 • Multiple time points for assessments of psychological well-being; in early pregnancy,
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34 late pregnancy and three months postpartum
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38 • Limited number of participants
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40 • Low adherence to the exercise intervention
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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 active²⁵, 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

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

15 **Trial design**

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

40 We included women with pre-pregnancy body mass index (BMI) ≥ 28 kg/m², ≥ 18 year, in
41 gestational week 12-18, carrying a singleton live foetus at an 11-14 week ultrasound scan.
42 Participants had to attend assessments and exercise classes at St. Olavs hospital. We excluded
43 women with high risk of preterm birth, diseases that could interfere with participation, or if they
44 exercised twice or more weekly in the period before inclusion. The women received written
45 information and signed informed consent on behalf of themselves and their offspring before
46 inclusion into the trial. We recruited participants through invitations sent along with notices for
47 routine ultrasound scan appointments, information sent to general practitioners, and through
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3 Google advertisements. At the last study visit, the women received infant food worth 500
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5 Norwegian kroner.
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8 **Intervention**

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10 All participants, regardless of group allocation, received maternity and postpartum care
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12 according to the Norwegian Standard Maternity Care for pregnant women, which is offered to
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14 all (free of charge).³⁶
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18 Women in the exercise group were offered supervised exercise sessions at St. Olavs
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20 hospital three times weekly from inclusion until delivery. The exercise program provided was
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22 in accordance with the recommendations from the American College of Obstetricians and
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24 Gynaecologists^{25,37,38} and from the Norwegian Directorate of Health for physical activity during
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26 pregnancy.³⁹ The exercise sessions were supervised by a physical therapist and consisted of 35
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28 minutes of treadmill walking at approximately 80% of maximal aerobic capacity
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30 (corresponding to Borg scale 12–15)³⁵ followed by 25 minutes of resistance training, including
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32 pelvic floor muscle training. In addition to the supervised program, we asked the women to
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34 exercise at home for 50 minutes twice weekly and to do daily pelvic floor muscle exercises. For
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36 a full description of the exercise intervention, see previous reports.^{32,35} Adherence to the
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38 exercise program was registered in a training diary. Women in the control group were not
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40 discouraged from physical activity or exercise.
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46 **Outcomes**

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48 Self-perceived psychological well-being was assessed by the “Psychological General Well-
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50 Being Index” (PGWBI) questionnaire⁴⁰ at baseline (gestational week 12-18), in late pregnancy
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52 (gestational week 34-37) and three months postpartum. Postpartum the participants also
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54 completed the “Edinburgh Postnatal Depression Scale” (EPDS) questionnaire.⁴¹ The women
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56 completed the questionnaires at the hospital while they underwent a 2 h oral glucose tolerance
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58 test, with trial researchers available to clarify questions if needed.
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3 The PGWBI questionnaire contains 22 questions regarding self-perceived psychological
4 health and general well-being, with both positive and negative affective states. The questions
5 are grouped into six intrapersonal states (subscales); “Anxiety”, “Depressed Mood”, “Positive
6 well-being”, “Self-control”, “General health”, and “Vitality”.⁴⁰ Each question has six response
7 alternatives where value 0 is given for the most negative option, and value 5 for the most
8 positive option. Depending of number of questions included, the range score in each subscale
9 is from 0 to 15, 20 or 25. The PGWBI global score ranges from 0 to 110, with higher scores
10 representing better psychological well-being.
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21 The EPDS contains 10 questions assessing how the woman is coping with life changes
22 related to pregnancy and childbirth. All questions contain four response alternatives. We
23 estimated total score with use of a scoring system 1-4, with “1” representing the most negative
24 option, and “4” the most positive option. A total score of <8 = “Depression not likely”, 9-11 =
25 “Depression possible”, 12-13 = “Fairly high possibility of depression”, ≥ 14 = “Probable
26 depression”. In addition, if the participant scored 1, 2 or 3 on question number 10, she was
27 classified as “Suicidal risk”.⁴¹
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37 Additionally, the participants reported their perceived health status at baseline and in
38 late pregnancy as either “very good”, “good”, “either good or bad”, “quite bad” or “bad”.
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43 **Sample size**

44 The sample size calculation for the ETIP trial was based on difference between groups in the
45 primary outcome (gestational weight gain) and is detailed elsewhere.^{32,35} We have not
46 performed a separate power calculation for the secondary analyses reported in this paper.
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53 **Randomization and blinding**

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

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10 We confirmed baseline data normality using Shapiro-Wilk tests and visual inspection of plots
11 and histograms. Comparisons between groups at baseline was analysed by independent samples
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13 t-tests and Fisher's Exact tests/Pearson Chi Square tests. We analysed between-groups
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15 differences in the effect of exercise training on psychological well-being (assessed by PGWBI)
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17 in late pregnancy and postpartum by general linear model analysis of covariance. Changes
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19 within-groups from baseline to late pregnancy and from late pregnancy to postpartum were also
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21 analysed by general linear model analysis of covariance. Baseline values were set as a covariate
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23 at late pregnancy analyses, and late pregnancy values were set as covariates at postpartum
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25 analyses. We analysed differences between groups in EDPS using an independent samples t-
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27 test. We assessed differences in baseline PGWBI between the participants who exercised per
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29 protocol and the non-adherent participants in the exercise group by independent samples t-tests.
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31 Due to the randomisation model, we assumed no systematic differences between groups at
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33 baseline. We based our primary analyses on the principle "intention to treat" and additionally
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35 performed "per protocol" analyses, according to pre-specified cut-off values for adherence to
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37 the exercise program.³⁵ No adjustment for multiple testing have been undertaken.
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45 We used IBM SPSS Statistics 23. We consider P -values < 0.05 as statistically
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47 significant.
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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 \pm 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)
	<i>Mean \pm SD/N (%)</i>	<i>Mean \pm SD/N (%)</i>
Age (years)	31.3 \pm 3.8	31.4 \pm 4.7
Body weight (kg)	95.3 \pm 12.8	98.3 \pm 14.2
Body mass index (kg/m²)	33.9 \pm 3.8	35.1 \pm 4.6
Weight classification		
Overweight, BMI 28.0–29.9 kg/m ²	3 (6.6)	5 (11.1)
Class 1 obesity, BMI 30.0–34.9 kg/m ²	28 (62.2)	19 (42.2)
Class 2 obesity, BMI 35.0–39.9 kg/m ²	11 (24.4)	15 (33.3)
Class 3 obesity, BMI \geq 40.0 kg/m ²	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)
\geq 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 \leq 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 \pm 11.1	76.2 \pm 14.3
Anxiety	19.8 \pm 3.3	19.2 \pm 4.6
Depressed mood	13.2 \pm 1.9	13.2 \pm 1.9
Positive well-being	12.2 \pm 2.8	12.6 \pm 3.1
Self-Control	12.9 \pm 1.7	12.0 \pm 2.5
General Health	9.7 \pm 2.8	9.5 \pm 2.7
Vitality	8.8 \pm 3.8	10.1 \pm 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					
		Score at baseline <i>N</i> = 91	Score late pregnancy <i>N</i> = 38	Score postpartum <i>N</i> = 36	Score late pregnancy <i>N</i> = 36	Score postpartum <i>N</i> = 34	Late pregnancy			Postpartum	
						<i>Diff</i>	<i>95% CI</i>	<i>P-value</i>	<i>Diff</i>	<i>95% CI</i>	<i>P-value</i>
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
<p><i>Missing late pregnancy:</i> Exercise 8, control, 5. <i>Missing postpartum:</i> Exercise 7, control 4. <i>Statistics:</i> 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).</p>											

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 woman 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 ≥ 28 kg/m²) 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

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3 trial. We had no information on previous mental health history or use of antidepressant
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5 treatment among the participants.
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8 **Comparison with other trials**

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11 Observational studies show that women who are physically active during pregnancy report
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13 better psychological well-being than less active women²⁸ and that the risk of psychological
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15 health problems increases in parallel to decreased exercise frequency during pregnancy.²⁷ A
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17 limited number of RCTs have investigated the effects of exercise training in pregnancy on
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19 psychological well-being, and the results diverge.^{29,30,45} Bogaerts and colleagues³⁰ showed
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21 reduced anxiety in late pregnancy among obese women who received an intervention
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23 combining regular motivational interviewing with advice about healthy eating and physical
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25 activity in pregnancy, compared to advice only or a standard care control group. They found,
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27 however, no effect of the intervention on depression.³⁰ In our study, the level of anxiety did not
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29 differ between groups in late pregnancy, but we observed a tendency of less symptoms of
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31 anxiety among the women who exercised per-protocol compared to the control group, which
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33 indicates a positive effect of regular exercise during pregnancy on risk of anxiety. Gustafsson
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35 and co-workers²⁹ investigated the effect of regular exercise during pregnancy on late pregnancy
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37 psychological well-being assessed by PGWBI. They included women in all BMI categories,
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39 but found, similar to our trial, no effect of exercise on mental health. In their trial, as in ours,
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41 the participants reported of good psychological well-being at baseline, contrast to previous
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43 studies showing a high prevalence (15-25%) of depression and anxiety among overweight and
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45 obese pregnant women^{2,7,8,46-49} and that especially the levels of anxiety increases from early to
46
47 late pregnancy in this population.⁴⁷ Compared to the general population of overweight and
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49 obese women, more women in our trial reported to fulfil the recommendations for physical
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51 activity during and after pregnancy,³² the number of pregnancy complications,³² were lower, and
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53 number of women exceeding the Institute of Medicine guidelines for gestational weight gain
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3 was also lower.^{32,33} All these factors are associated with increased risk for reduced
4 psychological well-being and could therefore explain stable PGWBI scores during pregnancy
5 in our study group. Again, this indicates that we included overweight and obese women with
6 good psychological well-being in our trial.
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12 We found no effect of exercise training on the risk for postnatal depression, which is in
13 line with previous studies suggesting limited effect of exercise interventions during pregnancy
14 on risk for depression after delivery.^{31,45} Our results show that few women who participated in
15 the trial reported of symptoms of postnatal depression. This is in contrast to a systematic review
16 and meta-analysis reporting a high risk of developing depression during the postpartum period
17 for women with pre-pregnancy obesity.¹ Also a cohort study by Ertel and colleagues,⁵ who
18 assessed postnatal depression among 1686 women in all BMI categories, found that pre-
19 pregnancy BMI >30 was associated with increased risk for depression six months postpartum.
20 The EDPS collects the woman's self-perceived psychological well-being during the last week,
21 and thereby the woman's current state of anxiety and depression. On the other hand, the "State
22 and Trait Anxiety Inventory (STAI)" questionnaire, assesses both short-term and long-term
23 symptoms, and might provide a different set of information compared to the EDPS. Even
24 though the EDPS is the most frequently used questionnaire for assessing risk for depression
25 postpartum, the type of questionnaires used in studies differs and this hampers comparison
26 between trials.
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46 **Generalizability and clinical implications**

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48 When compared to women in the Norwegian Medical Birth Registry,⁵⁰ the ETIP population is
49 representative for Norwegian overweight and obese pregnant women, according to BMI,
50 obesity grades I, II, III, age, education, parity and occupational activity/employment.³²
51 However, it is likely to believe that women who volunteered for participation in an exercise
52 trial are extra aware of possible benefits of maternal exercise, are more experienced with
53 physical activity and suffer from less pregnancy complications. We believe that the findings in
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3 our trial may be generalizable to relatively healthy pregnant women with pre-pregnancy BMI
4 of 28 or more.
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8 We based the trial intervention program on current recommendations for maternal
9 exercise and designed it for easy implementation into clinical practice. Health care
10 professionals, especially general practitioners and midwives who consult pregnant women, are
11 in a unique position to inform, help and guide overweight and obese women throughout
12 pregnancy. Clear recommendations for exercise and physical activity should be given to all
13 pregnant women, and the women should be closely monitored and motivated by maternal health
14 care personnel throughout pregnancy. Assessing psychological well-being early in pregnancy
15 may be important for prediction of adherence to exercise during pregnancy.
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26 **Conclusion**

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28 We found no statistically significant effects of supervised exercise training during pregnancy
29 on psychological well-being in late pregnancy or postpartum, nor on the prevalence of postnatal
30 depression, among overweight and obese women. Both groups reported good psychological
31 well-being and low risk for postnatal depression. The level of self-control early in pregnancy
32 may be important for exercise adherence during pregnancy. We need more research on the
33 preventive effect of exercise during pregnancy on maternal well-being, and on the factors
34 associated with motivation for exercise during pregnancy.
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3 **Word count:** 3357 words
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10 received infant food from Nestlé worth 500 Norwegian kroner.
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18 **Competing interest statement:** We declare no conflicts of interest.
19
20

21 **Data sharing statement:** Dataset available online alongside the article.
22
23

24
25 **Author Contributions:** KKG acquired the data, analysed the data, interpreted the data and
26 drafted the manuscript. ASH interpreted the data and critically revised the manuscript. SM
27 designed the study and critically revised the manuscript, SNS designed the study and critically
28 revised the manuscript, KÅS designed the study and critically revised the manuscript, TM
29 acquired some of the data, deigned the study and critically revised the manuscript. All authors
30 have approved the final version of the manuscript and are accountable for all aspects of the
31 work.
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40 **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.

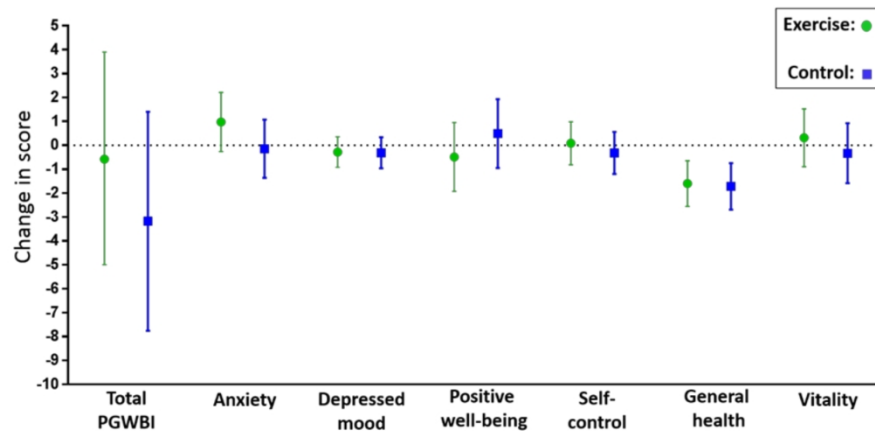


Figure 1. Change in the PGWBI global score and the six subscales from baseline to late pregnancy in the exercise group and the control group, presented as mean and 95% CI.

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.

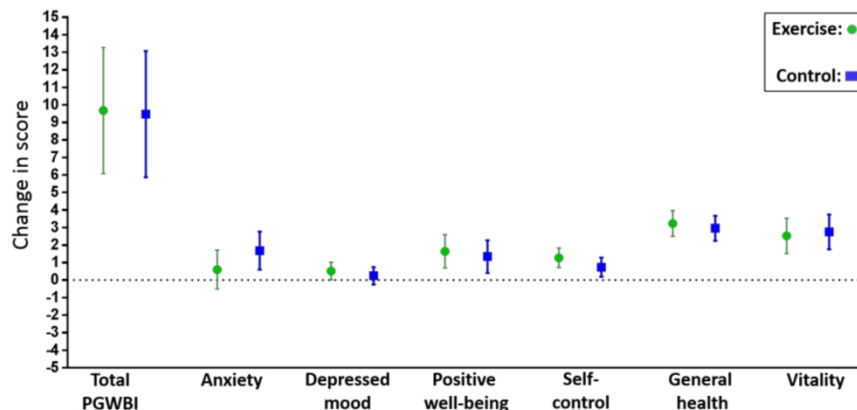


Figure 2. Change in the PGWBI global score and the six subscales from late pregnancy to three months postpartum in the exercise group and the control group, presented as mean and 95% CI.

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					
	Score late pregnancy <i>N</i> = 19	Score postpartum <i>N</i> = 19	Score late pregnancy <i>N</i> = 36	Score postpartum <i>N</i> = 34	Late pregnancy			Postpartum		
					<i>Diff</i>	<i>95% CI</i>	<i>P-value</i>	<i>Diff</i>	<i>95% CI</i>	<i>P-value</i>
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
<p><i>Missing late pregnancy:</i> Exercise 6, control, 5. <i>Missing postpartum:</i> Exercise 5, control 4. <i>Statistics:</i> 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).</p>										



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

1		assessing outcomes) and how	
2	11b	If relevant, description of the similarity of interventions	
3	Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes
4		12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses
5			
6	Results		
7	Participant flow (a	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and
8	diagram is strongly		were analysed for the primary outcome
9	recommended)	13b	For each group, losses and exclusions after randomisation, together with reasons
10	Recruitment	14a	Dates defining the periods of recruitment and follow-up
11		14b	Why the trial ended or was stopped
12	Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
13	Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was
14			by original assigned groups
15	Outcomes and	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its
16	estimation		precision (such as 95% confidence interval)
17		17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
18	Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing
19			pre-specified from exploratory
20	Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)
21			
22	Discussion		
23	Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
24	Generalisability	21	Generalisability (external validity, applicability) of the trial findings
25	Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
26			
27	Other information		
28	Registration	23	Registration number and name of trial registry
29	Protocol	24	Where the full trial protocol can be accessed, if available
30	Funding	25	Sources of funding and other support (such as supply of drugs), role of funders
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*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.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-028252.R1
Article Type:	Original research
Date Submitted by the Author:	17-Jun-2019
Complete List of Authors:	Garnæs, Kirsti; St. Olavs hospital , Department of Obstetrics and Gynaecology Helvik, AS; NTNU Fakultet for ingeniørvitenskap og teknologi Trondheim, Stafne, Signe; NTNU Fakultet for ingeniørvitenskap og teknologi Trondheim, Department of Public Health and General Practice Mørkved, Siv; the Central Norway Regional Health Authority; St. Olavs hospital Salvesen, Kjell; Trondheim University Hospital, Dept of Obstetrics and gynaecology Salvesen, Øyvind; Norwegian University of Science and Technology, Unit for Applied Clinical Research Moholdt, Trine; Norwegian University of Science and Technology,
Primary Subject Heading:	Sports and exercise medicine
Secondary Subject Heading:	General practice / Family practice, Mental health, Obstetrics and gynaecology, Sports and exercise medicine
Keywords:	maternal obesity, MENTAL HEALTH, Depression & mood disorders < PSYCHIATRY, Anxiety disorders < PSYCHIATRY, Pregnancy and exercise responses, Maternal health, mental health, depression, anxiety, pregnancy complications

SCHOLARONE™
Manuscripts

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5 2 **among overweight and obese women, secondary analyses of the ETIP-trial, a randomized**
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12 5 Kirsti Krohn Garnæs^{1,2}, Anne-Sofie Helvik^{3,4}, Signe Nilsen Stafne^{2,5}, Siv Mørkved^{2,4}, Kjell
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3 **Abstract**

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5 **Objectives:** Women with high body mass index (BMI) have increased risk for symptoms of
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7 anxiety and depression during pregnancy and postpartum. In this pre-specified secondary
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9 analysis from the Exercise Training in Pregnancy (ETIP) trial, our aim was to examine effects
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11 of supervised exercise during pregnancy on psychological well-being in late pregnancy and
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13 postpartum among women with a pre-pregnancy BMI ≥ 28 kg/m².
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16 **Design:** Single-centre, parallel group, randomized controlled trial.

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18 **Setting:** University Hospital, Norway

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20 **Participants:** Ninety-one women (age 31.2±4.1 years, BMI 34.5±4.2 kg/m²), 46 in the exercise
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22 group, 45 in the control group, were included in the trial.
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26 **Intervention:** The exercise group was offered three weekly supervised exercise sessions (35
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28 minutes of moderate intensity walking/running, and 25 minutes of resistance training), until
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30 delivery.
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33 **Primary and secondary outcomes measures:** Primary analyses were based on intention to
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35 treat, with secondary per-protocol analyses. To assess psychological well-being, we used the
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37 «Psychological General Well-Being Index» (PGWBI) at inclusion (gw. 12-18), late pregnancy
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39 (gw. 34-37), and three months postpartum. Postpartum, we assessed depression using the
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41 «Edinburgh Postnatal Depression Scale» (EDPS).
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45 **Results:** Numbers completed data collection: Late pregnancy 72 (exercise 38, control 36),
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47 postpartum 70 (exercise 36, control 34). In the exercise group, 50% adhered to the exercise
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49 protocol. Baseline PGWBI for all women was 76.4±12.6. Late pregnancy PGWBI; exercise
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51 76.6 (95% CI 72.2, 81.0), control 74.0 (95% CI 69.4, 78.5) ($p = 0.42$). Postpartum PGWBI;
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53 exercise 85.4 (95% CI 81.9, 88.8), control 84.6 (95% CI 80.8, 88.4) (with no between-group
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55 difference, $p = 0.77$). There was no between-group difference in EDPS; exercise 2.96 (95% CI
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57 1.7, 4.2), control 3.48 (95% CI 2.3, 4.7) ($p = 0.55$).
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3 52 **Conclusions:** We found no effect of supervised exercise training during pregnancy on
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5 53 psychological well-being among women with high BMI. Our findings may be hampered by low
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7 54 adherence to the exercise protocol.
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14 56 **Trial registration number:** ClinicalTrials.gov NCT01243554
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16 57 **Key words:** Maternal health, mental health, depression, anxiety, pregnancy complications
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24 60 **Article summary**
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27 62 **Strengths and limitations of this study:**
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30 63 • This study was a randomized controlled trial.
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32 64 • The exercise program was supervised.
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34 65 • The trial assessed psychological well-being at multiple time points; in early pregnancy,
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36 66 late pregnancy and three months postpartum
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38 67 • The trial was limited by lower number of participants than originally planned.
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40 68 • The trial was limited by relatively low adherence to the exercise intervention
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70 **Introduction**

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

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

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3 95 In the Exercise Training in Pregnancy (ETIP) trial, we determined the effect of offering
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5 96 supervised exercise training during pregnancy on maternal and foetal outcomes among 91
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8 97 women with overweight or obesity, with gestational weight gain as the primary outcome.³²⁻³⁵
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10 98 In this pre-specified³⁵ secondary analysis of the ETIP trial, we aimed to determine the effect of
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12 99 exercise training on self-perceived psychological well-being in late pregnancy and three months
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14 100 postpartum, and the effect of exercise training in pregnancy on the risk for postnatal depression.
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18 19 102 **Methods**

20 21 103 **Trial design**

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23 104 The ETIP trial was a single-centre, parallel-group RCT where we determined the effects of
24
25 105 offering overweight and obese women supervised exercise training during pregnancy compared
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27 106 to standard maternal care only. The trial was undertaken at the Norwegian University of Science
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29 107 and Technology (NTNU) and St. Olavs hospital, Trondheim University Hospital, Norway. We
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31 108 started inclusion in September 2010, with the last assessments in November 2015. The ETIP
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33 109 trial protocol and detailed description of the methods have been published elsewhere.^{32,35} The
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35 110 study was approved by the Regional Committee for Medical and Health Research Ethics (REK-
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37 111 midt 2010/1522) and registered in ClinicalTrials.gov (NCT01243554). The ETIP trial was
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39 112 submitted to Clinical Trials September 06, 2010 with the Study Start Date set to September
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41 113 2010 (Please see attached PRS Review Comments). Clinical Trials responded with a comment
42
43 114 that they wanted us to respond to and therefore did not release the trial immediately. Due to a
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45 115 delay at our Faculty's administration, the respond to the comment was not submitted until
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47 116 November 2010.
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118 **Participants**

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3 119 We included women with pre-pregnancy body mass index (BMI) ≥ 28 kg/m², ≥ 18 year, in
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5 120 gestational week 12-18, carrying a singleton live foetus at an 11–14 week ultrasound scan.
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7 121 Categorisation of overweight and obesity related to BMI, was based on the World Health
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9 122 Organization (WHO) classification system.³⁶ Pre-pregnancy BMI was based on self-reported
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11 123 information. Participants had to attend assessments and exercise classes at St. Olavs hospital.
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13 124 We excluded women with high risk of preterm birth, diseases that could interfere with
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15 125 participation, or if they exercised twice or more weekly in the period before inclusion. The
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17 126 women received written information and signed informed consent on behalf of themselves and
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19 127 their offspring before inclusion into the trial. We recruited participants through invitations sent
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21 128 along with notices for routine ultrasound scan appointments, information sent to general
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23 129 practitioners, and through Google advertisements. At the last study visit, the women received
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25 130 infant food worth 500 Norwegian kroner.
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31 **Intervention**

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33 132 All participants, regardless of group allocation, received maternity and postpartum care
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35 133 according to the Norwegian Standard Maternity Care for pregnant women, which is offered to
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37 134 all (free of charge).³⁷
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40 135 Women in the exercise group were offered supervised exercise sessions at St. Olavs
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42 136 hospital three times weekly from inclusion until delivery. The exercise program provided was
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44 137 in accordance with the recommendations from the American College of Obstetricians and
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46 138 Gynaecologists^{25,38,39} and from the Norwegian Directorate of Health for physical activity during
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48 139 pregnancy.⁴⁰ The exercise sessions were supervised by a physical therapist and consisted of 35
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50 140 minutes of treadmill walking at approximately 80% of maximal aerobic capacity
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52 141 (corresponding to Borg scale 12–15)³⁵ followed by 25 minutes of resistance training, including
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54 142 pelvic floor muscle training. In addition to the supervised program, we asked the women to
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56 143 exercise at home for 50 minutes at least once weekly, and to do daily pelvic floor muscle
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3 144 exercises. For a full description of the exercise intervention, see previous reports (Supplemental
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5 145 File 1.).^{32,35} Adherence to the exercise program was registered in a training diary. Women in
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7 146 the control group were not discouraged from physical activity or exercise.
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10 11 147 **Outcomes**

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13 148 Sociodemographic data was collected by self-reported questionnaires at baseline assessments.
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15 149 Information regarding the participants' psychological well-being and risk of postnatal
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17 150 depression was assessed by self-reported questionnaires, completed at the hospital while they
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19 151 underwent a 2 h oral glucose tolerance test at baseline, late pregnancy and three months
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21 152 postpartum, with trial researchers available to clarify questions if needed.
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25 153 Psychological well-being was assessed by the "Psychological General Well-Being
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27 154 Index" (PGWBI) questionnaire (PGWBI © 1984 Harold J. Dupuy, Mapi Research Trust)^{41,42} at
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29 155 baseline (gestational week 12-18), in late pregnancy (gestational week 34-37) and three months
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31 156 postpartum. The Psychological General Well-being (PGWB) scale measures the last week self-
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33 157 perceived psychological health and general well-being, and intends to assess health related
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35 158 quality of life or, said otherwise, to reflect a sense of well-being or distress that includes positive
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37 159 as well as negative intrapersonal affective or emotional states.³⁵ It consists of 22 items with a
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39 160 six-point self-response scale that ranges from zero (= most negative option) to five (= most
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41 161 positive option) and includes six non-overlapping dimensions: anxiety (five items), depressed
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43 162 mood (three items), positive well-being (four items), self-control (three items), general health
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45 163 (three items), and vitality (four items).^{35, 38} Each dimension is summed and the total (maximum
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47 164 = 110) forms the overall PGWBI. The anxiety dimension assessed whether the subjects were
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49 165 bothered by nervousness, were generally tense, anxious, worried or upset, and/or under stress
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51 166 strain or pressure. Depressed-mood measured if the participants were depressed, hopeless, or
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53 167 downhearted and 'blue'. Positive well-being indicated the general spirit, cheerfulness, or
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55 168 happiness and satisfaction with personal life. The self-control dimension intended to measure
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3 169 whether the subjects felt emotionally stable, in firm control, or afraid of losing control. General
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5 170 health assessed if the subjects were bothered with pain, disorder, or illness and whether they
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8 171 were healthy enough 'to do things.' Finally, vitality contained items that assessed the
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10 172 participants' energy, whether they felt active, vigorous, or sluggish, tired and worn out.³⁵
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13 173 The PGWBI questionnaire is a generic questionnaire frequent used in clinical trials
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15 174 across many conditions, and translated to several languages.⁴³⁻⁴⁶ The PGWBI has been found
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17 175 suitable for subjects 14-90 years and is a highly preferred self-administered inventory.³⁵ The
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19 176 internal consistency reliability is high with Cronbach's alpha correlations between 0.90 and
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21 177 0.94.³⁵ Similar correlations (Cronbach's alpha > 0.90) have been shown for tests done in
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23 178 Sweden,⁴³ with culture and language similar to the Norwegian,⁴⁴ and recently used by
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25 179 Gustafsson and colleges in a clinical trial among Norwegian pregnant women.²⁹ The present
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27 180 Norwegian version of the questionnaire was translated by a standard forward-backward method
28
29 181 at St. Olavs Hospital, the university Hospital, Trondheim, Norway, in February 2002.⁴⁷
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33 182 To measure the prevalence of symptoms of postnatal depression, the participants also
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35 183 completed the "Edinburgh Postnatal Depression Scale" (EPDS) questionnaire (Cox, Holden
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37 184 and Sagosky, 1987).⁴⁸ The questionnaire is a non-generic self-rating scale, which measures the
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39 185 presence of depressive symptoms during in the postpartum period, indicating how the mother
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41 186 has felt during the last week.^{48,49} The EPDS questionnaire contains 10 questions. All questions
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43 187 contain four response alternatives were the women are asked to "please underline the answer
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45 188 witch comes closest to how you have felt in the past 7 days".⁴⁸ We estimated total score of the
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47 189 ten items with use of a scoring system 0-3, with "0" representing the most negative option, and
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49 190 "3" the most positive option. Based on validations of the questionnaire,⁴⁸ we used a cut-off
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51 191 score of ≥ 10 indicating minor depression, ≥ 13 indicating a major depression. The EPDS
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53 192 questionnaire is developed and commonly used for measurement of depressive symptoms in
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55 193 the postpartum period, but is also used and validated for the pregnancy period.⁴⁸ The
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3 194 questionnaire is translated to Norwegian and found valid to detect postpartum depression in a
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5 195 Norwegian population.^{50,51}
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8 196 Additionally, the participants reported their self-perceived general health status at
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10 197 baseline and in late pregnancy as either “very good”, “good”, “either good or bad”, “quite bad”
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12 198 or “bad”. This question is taken from the SF 36 Short Form Health Survey. This survey is
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14 199 translated to Norwegian, and tested for reliability and validity in a Norwegian population.
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17 18 200 **Sample size**

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20 201 The sample size calculation for the ETIP trial was based on difference between groups in the
21
22 202 primary outcome, gestational weight gain from baseline assessments to delivery (Supplemental
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24 203 File 1.).^{32,35} Based on previous studies, a mean change of 6 kg was assumed as clinical
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26 204 relevant.^{52,53} A two-sided independent sample *t*-test with a 5 % level of significance, a standard
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28 205 deviation of 10, and a power of 0.90 defined our target study population to be 59 in each group.
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30 206 We estimated the dropout rate in the trial to be 15 %, and on basis of these estimations aimed
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32 207 to include 150 women. We have not performed a separate power calculation for the secondary
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34 208 analyses reported in this paper.
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41 210 **Randomization and blinding**

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43 211 Randomisation was performed after baseline assessments using a computer random number
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45 212 generator, developed and administrated at the Unit for Applied Clinical Research, NTNU. The
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47 213 personnel who provided the participants with questionnaires regarding psychological well-
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49 214 being in late pregnancy and postpartum were not blinded for group allocation. Further details
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51 215 about randomization and blinding in the ETIP trial are published previously.³²
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56 216 **Statistical methods**

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3 217 We confirmed baseline data normality using Shapiro-Wilk tests and visual inspection of plots
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5 218 and histograms. Comparisons between groups at baseline was analysed by independent samples
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7 219 t-tests and Fisher's Exact tests. We analysed between-groups differences in the effect of
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9 220 exercise training on psychological well-being (assessed by PGWBI) in late pregnancy and
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11 221 postpartum, and between-groups difference in "Self-perceived general health status" late
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13 222 pregnancy by general linear model analysis of covariance. Changes within-groups from
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15 223 baseline to late pregnancy and from late pregnancy to postpartum were also analysed by general
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17 224 linear model analysis of covariance. Baseline values were set as a covariate at late pregnancy
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19 225 analyses, and late pregnancy values were set as covariates at postpartum analyses. We analysed
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21 226 differences between groups in EDPS using an independent samples t-test. We assessed
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23 227 differences in baseline PGWBI between the participants who exercised per protocol and the
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25 228 non-adherent participants in the exercise group by independent samples t-tests. Due to the
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27 229 randomisation model, we assumed no systematic differences between groups at baseline. We
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29 230 based our primary analyses on the principle "intention to treat" and additionally performed "per
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31 231 protocol" analyses, according to pre-specified cut-off values for adherence to the exercise
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33 232 program (Supplemental File 1.).³⁵ No adjustment for multiple testing have been undertaken.

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39 233 We used IBM SPSS Statistics 23. We consider P -values < 0.05 as statistically
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41 234 significant.

42 43 44 235 **Patient and public involvement**

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47 236 No patients involved.
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237 **Results**

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

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

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

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

Subjects characteristics	Exercise Group (n = 46)	Control Group (n = 45)
	<i>Mean \pm SD/N (%)</i>	<i>Mean \pm SD/N (%)</i>
Age (years)	31.3 \pm 3.8	31.4 \pm 4.7
Body weight (kg)	95.3 \pm 12.8	98.3 \pm 14.2
Body mass index (kg/m²)	33.9 \pm 3.8	35.1 \pm 4.6
Weight classification		
Overweight, BMI 28.0–29.9 kg/m ²	3 (6.6)	5 (11.1)
Class 1 obesity, BMI 30.0–34.9 kg/m ²	28 (62.2)	19 (42.2)
Class 2 obesity, BMI 35.0–39.9 kg/m ²	11 (24.4)	15 (33.3)
Class 3 obesity, BMI \geq 40.0 kg/m ²	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)
\geq 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 \leq 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 \pm 11.1	76.2 \pm 14.3
Anxiety	19.8 \pm 3.3	19.2 \pm 4.6
Depressed mood	13.2 \pm 1.9	13.2 \pm 1.9
Positive well-being	12.2 \pm 2.8	12.6 \pm 3.1
Self-Control	12.9 \pm 1.7	12.0 \pm 2.5
General Health	9.7 \pm 2.8	9.5 \pm 2.7
Vitality	8.8 \pm 3.8	10.1 \pm 3.4

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3 *Missing:* Education: Control: 1. General health status: Control: 3. PGWBI: Exercise; 2,
4 control; 4.
5 *Statistics:* Baseline variables were analysed by Independent samples t-test, and Fisher's
6 Exact Test.
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265 **Psychological well-being in late pregnancy**

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

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

281 **Psychological well-being three months postpartum**

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

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3 286 significant differences in any of the six subscales (Supplementary Table 1). Figure 3 illustrates
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5 287 the changes in PGWBI global score and subscales from late pregnancy to postpartum in each
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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					
		Score at baseline <i>N</i> = 91	Score late pregnancy <i>N</i> = 38	Score postpartum <i>N</i> = 36	Score late pregnancy <i>N</i> = 36	Score postpartum <i>N</i> = 34	Late pregnancy			Postpartum	
						<i>Diff</i>	95% CI	<i>P</i> -value	<i>Diff</i>	95% CI	<i>P</i> -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

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

295 We found no statistically significant difference in total EPDS score three months postpartum
296 between the exercise (2.96, 95% CI 1.7, 4.2) and control group (3.48, 95% CI 2.3, 4.7) ($p =$
297 0.55). No women in either the exercise group or the control group reported of a total EPDS
298 score of 13 or more, representing indication of major depression. Two women (7.1%) in the
299 exercise group and three women (10.3%) in the control group reported at total EPDS score
300 between 10 and 12, representing indication of a minor depression. When analysing per-
301 protocol, no statistical significant difference in total EPDS score was found between the
302 exercise group (2.38, 95% CI 1.72, 4.2) and the control group (3.48, 95% CI 2.3, 4.7) ($p = 0.30$).

303 **Baseline comparison within the exercise group**

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

308 **Harms**

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

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313

314 **Discussion**

315 **Main findings**

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

326 **Strengths and weaknesses of the study**

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

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

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

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3 339 the control group might have reduced the chance of finding an effect of the intervention. Our
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5 340 trial included comprehensive health assessments and close monitoring of the women, regardless
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7 341 of group allocation. This close follow-up by health personnel may have prevented reduced
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9 342 psychological well-being among all the women in the trial. We had no information on previous
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11 343 mental health history or use of antidepressant treatment among the participants.
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15 344 **Comparison with other trials**

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17 345 Observational studies show that women who are physically active during pregnancy report
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19 346 better psychological well-being than less active women²⁸ and that the risk of psychological
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21 347 health problems increases in parallel to decreased exercise frequency during pregnancy.²⁷ A
22
23 348 limited number of RCTs have investigated the effects of exercise training in pregnancy on
24
25 349 psychological well-being, and the results diverge.^{29,30,57} Bogaerts and colleagues³⁰ showed
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27 350 reduced anxiety in late pregnancy among obese women who received an intervention
28
29 351 combining regular motivational interviewing with advice about healthy eating and physical
30
31 352 activity in pregnancy, compared to advice only or a standard care control group. They found,
32
33 353 however, no effect of the intervention on depression.³⁰ In our study, the level of anxiety did not
34
35 354 differ between groups in late pregnancy, but we observed a tendency of less symptoms of
36
37 355 anxiety among the women who exercised per-protocol compared to the control group, which
38
39 356 indicates a positive effect of regular exercise during pregnancy on risk of anxiety. Gustafsson
40
41 357 and co-workers²⁹ investigated the effect of regular exercise during pregnancy on late pregnancy
42
43 358 psychological well-being assessed by PGWBI. They included women in all BMI categories,
44
45 359 but found, similar to our trial, no effect of exercise on mental health. In their trial, as in ours,
46
47 360 the participants reported of good psychological well-being at baseline, contrast to previous
48
49 361 studies showing a high prevalence (15-25%) of depression and anxiety among overweight and
50
51 362 obese pregnant women^{2,7,8,58-61} and that especially the levels of anxiety increases from early to
52
53 363 late pregnancy in this population.⁵⁹ Compared to the general population of women who are
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3 364 overweight or obese, more women in our trial reported to fulfil the recommendations for
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5 365 physical activity during and after pregnancy,³² the number of pregnancy complications were
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7 366 lower, and number of women exceeding the Institute of Medicine guidelines for gestational
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10 367 weight gain was also lower.^{32,33} All these factors are associated with increased risk for reduced
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12 368 psychological well-being and could therefore explain stable PGWBI scores during pregnancy
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14 369 in our study group. Again, this indicates that we included women with good psychological well-
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17 370 being in our trial.

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19 371 We found no effect of exercise training on the risk for postnatal depression, which is in
20
21 372 line with previous studies suggesting limited effect of exercise interventions during pregnancy
22
23 373 on risk for depression after delivery.^{31,57} Our results show that few women who participated in
24
25 374 the trial reported of symptoms of postnatal depression. This is in contrast to a systematic review
26
27 375 and meta-analysis reporting a high risk of developing depression during the postpartum period
28
29 376 for women with pre-pregnancy obesity.¹ Also a cohort study by Ertel and colleagues,⁵ who
30
31 377 assessed postnatal depression among 1686 women in all BMI categories, found that pre-
32
33 378 pregnancy BMI >30 was associated with increased risk for depression six months postpartum.
34
35 379 The EDPS collects the woman's self-perceived psychological well-being during the last week,
36
37 380 and thereby the woman's current state of anxiety and depression. On the other hand, the "State
38
39 381 and Trait Anxiety Inventory (STAI)" questionnaire, assesses both short-term and long-term
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41 382 symptoms, and might provide a different set of information compared to the EDPS. Even
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43 383 though the EDPS is the most frequently used questionnaire for assessing risk for depression
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45 384 postpartum, the type of questionnaires used in studies differs and this hampers comparison
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47 385 between trials.

386 **Generalizability and clinical implications**

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

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3 390 However, it is likely to believe that women who volunteered for participation in an exercise
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5 391 trial are extra aware of possible benefits of maternal exercise, are more experienced with
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7 392 physical activity and suffer from less pregnancy complications. We believe that the findings in
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10 393 our trial may be generalizable to relatively healthy pregnant women with pre-pregnancy BMI
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12 394 of 28 or more.

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14 395 We based the trial intervention program on current recommendations for maternal
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16 396 exercise and designed it for easy implementation into clinical practice. Health care
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18 397 professionals, especially general practitioners and midwives who consult pregnant women, are
19
20 398 in a unique position to inform, help and guide women with high BMI throughout pregnancy.
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22 399 Clear recommendations for exercise and physical activity should be given to all pregnant
23
24 400 women, and the women should be closely monitored and motivated by maternal health care
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26 401 personnel throughout pregnancy. Assessing psychological well-being early in pregnancy may
27
28 402 be important for prediction of adherence to exercise during pregnancy.

33 403 **Conclusion**

34
35 404 We found no statistically significant effects of supervised exercise training during pregnancy
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37 405 on psychological well-being in late pregnancy or postpartum, nor on the prevalence of
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39 406 symptoms of postnatal depression, among women with overweight or obese women. Both
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41 407 groups reported good psychological well-being and low risk for postnatal depression. The level
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43 408 of self-control early in pregnancy may be important for exercise adherence during pregnancy.
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45 409 Low adherence to the exercise protocol may have reduced the chance of finding an effect of
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47 410 regular maternal exercise on mental health.

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52 411 We need high sample-size trials with sufficient adherence to intervention protocols to be able
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54 412 to investigate the true effect of exercise during pregnancy on maternal well-being, and to
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56 413 examine factors associated with motivation for exercise during pregnancy.
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12
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20
21 426 Circulation and Medical imaging, Faculty of Medicine, NTNU, Norway. ORCID: 0000-0002-
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23 427 0983-8702.
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26
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28
29 429 drafted the manuscript. ASH interpreted the data and critically revised the manuscript. SM
30
31 430 designed the study and critically revised the manuscript, SNS designed the study and critically
32
33 431 revised the manuscript, KÅS designed the study and critically revised the manuscript, ØS
34
35 432 provided the statistics in previous published papers in the ETIP trial, and reviewed statistical
36
37 433 methods in the current manuscript, TM acquired some of the data, deigned the study and
38
39 434 critically revised the manuscript. All authors have approved the final version of the manuscript
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41 435 and are accountable for all aspects of the work.
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3 609 **Figure legends**
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6 610 **Figure 1.** CONSORT flow chart ETIP trial.
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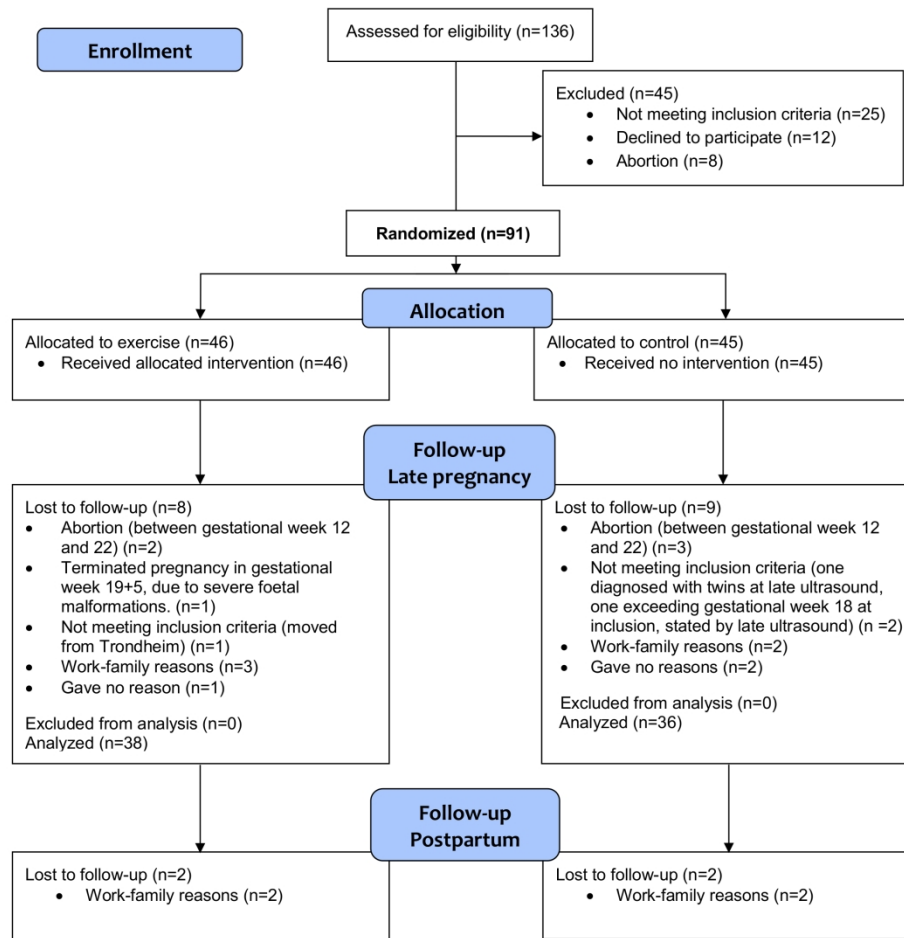
10 612 **Figure 2.** Changes in the Psychological General Well-Being Index (PGWBI) global score and
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12 the six subscales from baseline to late pregnancy in the exercise group and the control group.
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14 Data are means with 95% confidence intervals.
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19 616 **Figure 3.** Changes in the Psychological General Well-Being Index (PGWBI) global score and
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21 the six subscales from late pregnancy to postpartum in the exercise group and the control group.
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23 Data are means with 95% confidence intervals.
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CONSORT Flow Diagram



CONSORT Flow chart ETIP trial

209x229mm (300 x 300 DPI)

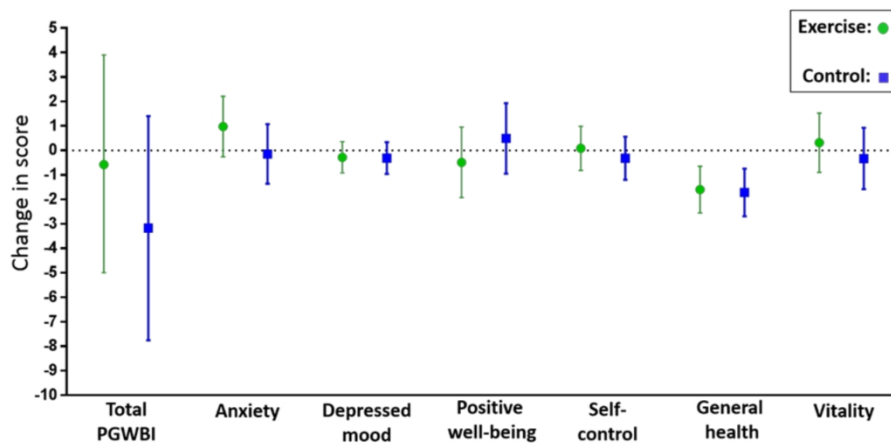


Figure 2. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from baseline to late pregnancy in the exercise group and the control group. Data are means with 95% confidence intervals.

168x88mm (300 x 300 DPI)

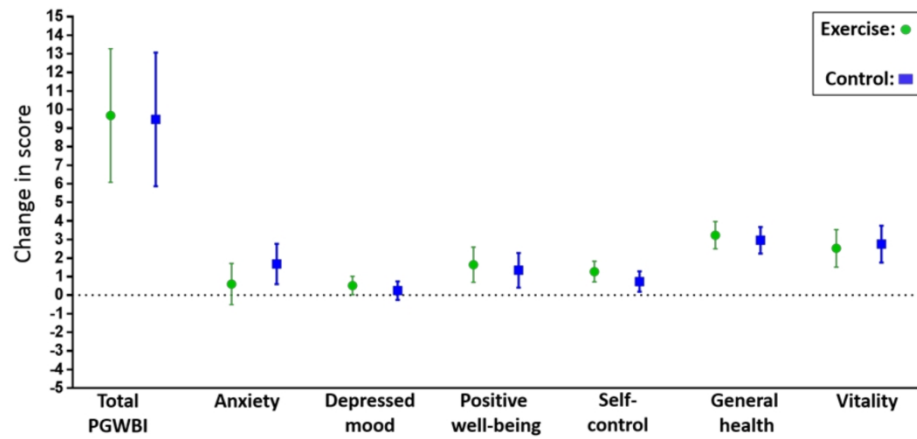


Figure 3. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from late pregnancy to postpartum in the exercise group and the control group. Data are means with 95% confidence intervals.

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					
	Score late pregnancy <i>N</i> = 19	Score postpartum <i>N</i> = 19	Score late pregnancy <i>N</i> = 36	Score postpartum <i>N</i> = 34	Late pregnancy			Postpartum		
					<i>Diff</i>	<i>95% CI</i>	<i>P-value</i>	<i>Diff</i>	<i>95% CI</i>	<i>P-value</i>
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
<p><i>Missing late pregnancy:</i> Exercise 6, control, 5. <i>Missing postpartum:</i> Exercise 5, control 4. <i>Statistics:</i> 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).</p>										



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.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-028252.R2
Article Type:	Original research
Date Submitted by the Author:	16-Sep-2019
Complete List of Authors:	Garnæs, Kirsti; St. Olavs Hospital University Hospital, Trondheim, Norway, Department of Obstetrics and Gynaecology; NTNU Faculty of Medicine and Health Sciences, Department of Public Health and Nursing Helvik, AS; NTNU Faculty of Medicine and Health Sciences, General Practice Research Unit, Department of Public Health and Nursing Stafne, Signe; NTNU Faculty of Medicine and Health Sciences, Department of Public Health and Nursing; St. Olavs hospital, Trondheim University Hospital, Clinical Services Mørkved, Siv; the Central Norway Regional Health Authority; St. Olavs hospital Salvesen, Kjell; St. Olavs Hospital, Trondheim University Hospital, Norway, Department of Obstetrics and Gynaecology; NTNU Faculty of Medicine and Health Sciences, Department of Clinical and Molecular Medicine Salvesen, Øyvind; NTNU Faculty of Medicine and Health Sciences, Department of Public Health and Nursing Moholdt, Trine; NTNU Faculty of Medicine and Health Sciences, Department of Circulation and Medical Imaging
Primary Subject Heading:	Sports and exercise medicine
Secondary Subject Heading:	General practice / Family practice, Mental health, Obstetrics and gynaecology, Sports and exercise medicine
Keywords:	maternal obesity, MENTAL HEALTH, Depression & mood disorders < PSYCHIATRY, Anxiety disorders < PSYCHIATRY, Pregnancy and exercise responses, Maternal health, mental health, depression, anxiety, pregnancy complications

SCHOLARONE™
Manuscripts

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3 1 **Effects of supervised exercise training during pregnancy on psychological well-being**
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5 2 **among overweight and obese women: Secondary analyses of the ETIP-trial, a randomized**
6
7 3 **controlled trial.**
8
9

10 4
11
12 5 Kirsti Krohn Garnæs^{1,2}, Anne-Sofie Helvik^{3,4}, Signe Nilsen Stafne^{2,5}, Siv Mørkved^{2,4}, Kjell
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14 6 Åsmund Salvesen,^{1,6} Øyvind Salvesen,² Trine Moholdt⁷
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1
2
3 **Abstract**

4
5 **Objectives:** Women with high body mass index (BMI) have increased risk for symptoms of
6
7 anxiety and depression during pregnancy and postpartum. In this pre-specified secondary
8
9 analysis from the ETIP trial, our aim was to examine effects of supervised exercise during
10
11 pregnancy on psychological well-being in late pregnancy and postpartum among women with
12
13 a pre-pregnancy BMI ≥ 28 kg/m².
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15

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

17
18 **Setting:** University Hospital, Norway

19
20 **Participants:** Ninety-one women (age 31.2 \pm 4.1 years, BMI 34.5 \pm 4.2 kg/m²), 46 in the exercise
21
22 group, 45 in the control group, were included in the trial.
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25
26 **Intervention:** The exercise group was offered three weekly supervised exercise sessions (35
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28 minutes of moderate intensity walking/running and 25 minutes of resistance training), until
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30 delivery.
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33 **Primary and secondary outcomes measures:** Primary analyses were based on intention to
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35 treat, with secondary per-protocol analyses. To assess psychological well-being, we used the
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37 «Psychological General Well-Being Index» (PGWBI) at inclusion (gestational week 12-18),
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39 late pregnancy (gestational week 34-37), and three months postpartum. We assessed postpartum
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41 depression using the «Edinburgh Postnatal Depression Scale» (EDPS).
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45 **Results:** Numbers completed data collection: Late pregnancy 72 (exercise 38, control 36),
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47 postpartum 70 (exercise 36, control 34). In the exercise group, 50% adhered to the exercise
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49 protocol. Baseline PGWBI for all women was 76.4 \pm 12.6. Late pregnancy PGWBI; exercise
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51 76.6 (95% CI 72.2, 81.0), control 74.0 (95% CI 69.4, 78.5) ($p = 0.42$). Postpartum PGWBI;
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53 exercise 85.4 (95% CI 81.9, 88.8), control 84.6 (95% CI 80.8, 88.4) (with no between-group
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55 difference, $p = 0.77$). There was no between-group difference in EDPS; exercise 2.96 (95% CI
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57 1.7, 4.2), control 3.48 (95% CI 2.3, 4.7) ($p = 0.55$).
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3 52 **Conclusions:** We found no effect of supervised exercise during pregnancy on psychological
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5 53 well-being among women with high BMI. Our findings may be hampered by low adherence to
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7 54 the exercise protocol.
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14 56 **Trial registration number:** ClinicalTrials.gov NCT01243554
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16 57 **Key words:** Maternal health, mental health, depression, anxiety, pregnancy complications
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24 60 **Article summary**
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26 61

27 62 **Strengths and limitations of this study:**
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- 29
30 63 • This study was a randomized controlled trial.
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32 64 • The exercise program was supervised.
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34 65 • The trial assessed psychological well-being at multiple time points; in early pregnancy,
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36 66 late pregnancy and three months postpartum.
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38 67 • The trial was limited by a lower number of participants than originally planned.
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40 68 • The trial was limited by relatively low adherence to the exercise intervention.
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70 **Introduction**

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

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

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3 95 In the Exercise Training in Pregnancy (ETIP) trial, we determined the effect of offering
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5 96 supervised exercise training during pregnancy on maternal and foetal outcomes among 91
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8 97 women with overweight or obesity, where gestational weight gain was our primary outcome
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10 98 measure.³²⁻³⁵ In this pre-specified³⁵, secondary analysis of the ETIP trial, we aimed to determine
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12 99 the effect of exercise training on self-perceived psychological well-being in late pregnancy and
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15 100 three months postpartum, and the effect of exercise training in pregnancy on the risk for
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17 101 postnatal depression.
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21 103 **Methods**

23 104 **Trial design**

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26 105 The ETIP trial was a single-centre, parallel-group RCT where we determined the effects of
27
28 106 offering overweight and obese women supervised exercise training during pregnancy compared
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30 107 to standard maternal care only. The trial was undertaken at the Norwegian University of Science
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32 108 and Technology (NTNU) and St. Olavs hospital, Trondheim University Hospital, Norway. We
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34 109 started inclusion of participants in September 2010, with the last assessments in November
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36 110 2015. The ETIP trial protocol and detailed description of the methods have been published
37
38 111 elsewhere.^{32,35} The study was approved by the Regional Committee for Medical and Health
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40 112 Research Ethics (REK-midt 2010/1522) and registered in ClinicalTrials.gov (NCT01243554).
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42 113 The ETIP trial was submitted to Clinical Trials September 06, 2010 with the Study Start Date
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44 114 set to September 2010 (Please see attached PRS Review Comments). Clinical Trials responded
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46 115 with a comment that they wanted us to respond to, and therefore did not release the trial
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48 116 immediately. Due to a delay at our Faculty's administration, the response to the comment was
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50 117 not submitted until November 2010.
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58 119 **Participants**

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3 120 We included women with pre-pregnancy body mass index (BMI) ≥ 28 kg/m², ≥ 18 year, in
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5 121 gestational week 12-18, and carrying a singleton live foetus at an 11–14 week ultrasound scan.
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7 122 Categorisation of overweight and obesity was based on the World Health Organization (WHO)
8
9 123 classification system.³⁶ Pre-pregnancy BMI was self-reported. Participants had to attend
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11 124 assessments and exercise classes at St. Olavs hospital. Our exclusion criteria were: high risk of
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13 125 preterm birth, diseases that could interfere with participation, habitual exercise training at
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15 126 baseline (defined as exercising twice or more weekly in the period before inclusion). The
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17 127 women received written information and signed informed consent on behalf of themselves and
18
19 128 their offspring before inclusion. We recruited participants through invitations sent along with
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21 129 notices for routine ultrasound scan appointments, information sent to general practitioners, and
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23 130 through Google advertisements. At the last study visit, the women received infant food worth
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25 131 500 Norwegian kroner.

31 132 **Intervention**

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33 133 All participants, regardless of group allocation, received maternity and postpartum care
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35 134 according to the Norwegian Standard Maternity Care for pregnant women, which is offered to
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37 135 all (free of charge).³⁷

38
39 136 Women in the exercise group were offered supervised exercise sessions at St. Olavs
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41 137 hospital three times weekly from inclusion until delivery. The exercise program was in
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43 138 accordance with the recommendations from the American College of Obstetricians and
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45 139 Gynaecologists^{25,38,39} and from the Norwegian Directorate of Health for physical activity during
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47 140 pregnancy.⁴⁰ The exercise sessions were supervised by a physical therapist and consisted of 35
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49 141 minutes of treadmill walking at approximately 80% of maximal aerobic capacity
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51 142 (corresponding to Borg scale 12–15)³⁵ followed by 25 minutes of resistance training, including
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53 143 pelvic floor muscle training. In addition to the supervised program, we asked the women to
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55 144 exercise at home for 50 minutes at least once weekly, and to do daily pelvic floor muscle
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3 145 exercises. For a full description of the exercise intervention, see previous reports
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5 146 (Supplementary File 1).^{32,35} Adherence to the exercise program was registered in a training
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7 147 diary. Women in the control group were not discouraged from physical activity or exercise.
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10 11 148 **Outcomes**

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13 149 Sociodemographic data was collected by self-reported questionnaires at baseline assessments.
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15 150 Information regarding the participants' psychological well-being and risk of postnatal
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17 151 depression was assessed by self-reported questionnaires, completed at the hospital while they
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19 152 underwent a 2 h oral glucose tolerance test at baseline, late pregnancy and three months
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21 153 postpartum, with trial researchers available to clarify questions if needed.
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25 154 Psychological well-being was assessed by the "Psychological General Well-Being
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27 155 Index" (PGWBI) questionnaire (PGWBI © 1984 Harold J. Dupuy, Mapi Research Trust)^{41,42} at
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29 156 baseline (gestational week 12-18), in late pregnancy (gestational week 34-37) and three months
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31 157 postpartum. PGWBI measures the last week self-perceived psychological health and general
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33 158 well-being, and intends to assess health related quality of life or, said otherwise, to reflect a
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35 159 sense of well-being or distress that includes positive and negative intrapersonal affective or
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37 160 emotional states.³⁵ PGWBI consists of 22 items with six-point self-response scales that range
38
39 161 from zero (= most negative option) to five (= most positive option). The questionnaire includes
40
41 162 six non-overlapping dimensions: anxiety (five items), depressed mood (three items), positive
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43 163 well-being (four items), self-control (three items), general health (three items), and vitality (four
44
45 164 items).^{35, 38} Each dimension is summed and the total (maximum = 110) forms the overall
46
47 165 PGWBI. The anxiety dimension assesses whether the subjects are bothered by nervousness,
48
49 166 were generally tense, anxious, worried or upset, and/or under stress strain or pressure.
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51 167 Depressed-mood assesses if the participants are depressed, hopeless, or downhearted and 'blue'.
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53 168 Positive well-being indicates the general spirit, cheerfulness, or happiness and satisfaction with
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55 169 personal life. The self-control dimension intends to measure whether the subjects feel
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3 170 emotionally stable, in firm control, or afraid of losing control. The general health dimension
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5 171 assesses if the subjects are bothered with pain, disorder, or illness and whether they are healthy
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7 172 enough 'to do things.' Finally, the vitality dimension contains items that assess the participants'
8
9 173 energy, whether they feel active, vigorous, or sluggish, tired and worn out.³⁵

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13 174 The PGWBI questionnaire is a generic questionnaire frequently used in clinical trials
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15 175 across many conditions, and translated to several languages.⁴³⁻⁴⁶ The PGWBI has been found
16
17 176 suitable for subjects 14-90 years and is a highly preferred self-administered inventory.³⁵ The
18
19 177 internal consistency reliability is high, with Cronbach's alpha correlations between 0.90 and
20
21 178 0.94.³⁵ Similar correlations (Cronbach's alpha > 0.90) have been shown for tests done in
22
23 179 Sweden,⁴³ with culture and language similar to the Norwegian,⁴⁴ and recently used by
24
25 180 Gustafsson and colleagues in a clinical trial among Norwegian pregnant women.²⁹ The present
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27 181 Norwegian version of the questionnaire was translated by a standard forward-backward method
28
29 182 at St. Olavs Hospital, the university Hospital, Trondheim, Norway, in February 2002.⁴⁷

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31
32
33 183 To measure the prevalence of symptoms of postnatal depression, the participants also
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35 184 completed the "Edinburgh Postnatal Depression Scale" (EPDS) questionnaire (Cox, Holden
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37 185 and Sagosky, 1987).⁴⁸ The EPDS questionnaire is a non-generic self-rating scale, which
38
39 186 measures the presence of depressive symptoms during the postpartum period, indicating how
40
41 187 the mother has felt during the last week.^{48,49} The EPDS questionnaire contains 10 questions. All
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43 188 questions contain four response alternatives were the women are asked to "please underline the
44
45 189 answer which comes closest to how you have felt in the past 7 days".⁴⁸ We estimated total score
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47 190 of the ten items using a scoring system from 0 to 3, with 0 representing the most negative option,
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49 191 and 3 the most positive option. Based on validations of the questionnaire,⁴⁸ we used a cut-off
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51 192 score of 10-12 as indication of minor depression and ≥ 13 as indication of major depression.
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53 193 The EPDS questionnaire is developed and commonly used for measurement of depressive
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55 194 symptoms in the postpartum period, but is also used and validated for the pregnancy period.⁴⁸
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3 195 The questionnaire is translated to Norwegian and valid to detect postpartum depression in a
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5 196 Norwegian population.^{50,51}
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8 197 Additionally, the participants reported their self-perceived general health status at
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10 198 baseline and in late pregnancy as either “very good”, “good”, “either good or bad”, “quite bad”
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12 199 or “bad”. This question is taken from the SF 36 Short Form Health Survey. This survey is
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14 200 translated to Norwegian and tested for reliability and validity in a Norwegian population.
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17 18 201 **Sample size**

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20 202 The sample size calculation for the ETIP trial was based on difference between groups in the
21
22 203 primary outcome, gestational weight gain from baseline assessments to delivery (Supplemental
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24 204 File 1.).^{32,35} Based on previous studies, a mean change of 6 kg was assumed as clinically
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26 205 relevant.^{52,53} A two-sided, independent samples *t*-test with 5 % level of significance, standard
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28 206 deviation of 10, and a power of 0.90 defined our target study population of 59 in each group.
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30 207 We estimated the dropout rate in the trial to be 15 %, and on basis of these estimations aimed
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32 208 to include 150 women. We have not performed a separate power calculation for the secondary
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34 209 analyses reported in this paper.
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41 211 **Randomization and blinding**

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43 212 Randomisation was performed after baseline assessments using a computer random number
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45 213 generator, developed and administrated at the Unit for Applied Clinical Research, NTNU. The
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47 214 personnel who provided the participants with questionnaires regarding psychological well-
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49 215 being in late pregnancy and postpartum were not blinded for group allocation. Further details
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51 216 about randomization and blinding in the ETIP trial are published previously.³²
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56 217 **Statistical methods**

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3 218 We confirmed baseline data normality using Shapiro-Wilk tests and visual inspection of plots
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5 219 and histograms. Comparisons between groups at baseline were analysed by independent
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7 220 samples t-tests and Fisher's Exact tests. We analysed between-groups differences in the effect
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9 221 of exercise training on psychological well-being (assessed by PGWBI) in late pregnancy and
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11 222 postpartum, and between-groups difference in "Self-perceived general health status" in late
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13 223 pregnancy by general linear model analysis of covariance. Changes within-groups from
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15 224 baseline to late pregnancy and from late pregnancy to postpartum were also analysed by general
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17 225 linear model analysis of covariance. Baseline values of each outcome were set as covariates in
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19 226 late pregnancy analyses, and late pregnancy values were set as covariates in postpartum
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21 227 analyses. We analysed differences between groups in EDPS using an independent samples t-
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23 228 test. We assessed differences in baseline PGWBI between the participants who exercised per
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25 229 protocol and the non-adherent participants in the exercise group by independent samples t-tests.
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27 230 Due to the randomisation model, we assumed no systematic differences between groups at
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29 231 baseline. We based our primary analyses on the "intention to treat" principle and additionally
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31 232 performed "per protocol" analyses, according to pre-specified cut-off values for adherence to
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33 233 the exercise program (Supplemental File 1.).³⁵ No adjustment for multiple testing have been
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35 234 undertaken.

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42 235 We used IBM SPSS Statistics 23 and considered P -values < 0.05 as statistically
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44 236 significant.

45 46 47 237 **Patient and public involvement**

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49 238 No patients involved.
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239 **Results**

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

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

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

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

Subjects characteristics	Exercise Group (n = 46)	Control Group (n = 45)
	<i>Mean \pm SD/N (%)</i>	<i>Mean \pm SD/N (%)</i>
Age (years)	31.3 \pm 3.8	31.4 \pm 4.7
Body weight (kg)	95.3 \pm 12.8	98.3 \pm 14.2
Body mass index (kg/m²)	33.9 \pm 3.8	35.1 \pm 4.6
Weight classification		
Overweight, BMI 28.0–29.9 kg/m ²	3 (6.6)	5 (11.1)
Class 1 obesity, BMI 30.0–34.9 kg/m ²	28 (62.2)	19 (42.2)
Class 2 obesity, BMI 35.0–39.9 kg/m ²	11 (24.4)	15 (33.3)
Class 3 obesity, BMI \geq 40.0 kg/m ²	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)
\geq 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 \leq 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 \pm 11.1	76.2 \pm 14.3
Anxiety	19.8 \pm 3.3	19.2 \pm 4.6
Depressed mood	13.2 \pm 1.9	13.2 \pm 1.9
Positive well-being	12.2 \pm 2.8	12.6 \pm 3.1
Self-Control	12.9 \pm 1.7	12.0 \pm 2.5
General Health	9.7 \pm 2.8	9.5 \pm 2.7
Vitality	8.8 \pm 3.8	10.1 \pm 3.4

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3 *Missing:* Education: Control: 1. General health status: Control: 3. PGWBI: Exercise; 2,
4 control; 4.
5 *Statistics:* Baseline variables were analysed by Independent samples t-test, and Fisher's
6 Exact Test.
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267 **Psychological well-being in late pregnancy**

268 We did not find any statistically significant difference between the groups in PGWBI global
269 score, nor in any of the six subscales, in late pregnancy (Table 2). In the per-protocol analyses
270 in late pregnancy, PGWBI global score was 80.2 (95% CI 73.9, 86.6) in participants who
271 adhered to the exercise program in the exercise group versus 74.7 (95% CI 70.4, 79.0) in the
272 control group ($p = 0.15$) (Supplementary Table 1). There were no statistically significant
273 between-group differences in the per-protocol analyses, , but a tendency of higher “Anxiety”
274 score in the per-protocol exercise group (21.4, 95% CI 19.7,23.2) compared to the control group
275 (19.5, 95% CI 18.4, 20.7) ($p = 0.07$) (Supplementary Table 1). Figure 2 illustrates the changes
276 in PGWBI global score and subscales from baseline to late pregnancy in each group.

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

283 **Psychological well-being three months postpartum**

284 There were no statistically significant differences between the groups in PGWBI global score,
285 nor in any of the six subscales three months postpartum (Table 2). In the postpartum per-
286 protocol analyses, PGWBI global score among women who adhered to the exercise program in
287 the exercise group was of 84.8 (95% CI 79.5, 90.2), versus 85.3 (95% CI 81.5, 89.2) in the
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3 288 control group ($p = 0.88$), with no statistically significant differences in any of the six subscales
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5 289 (Supplementary Table 1). Figure 3 illustrates the changes in PGWBI global score and subscales
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8 290 from late pregnancy to postpartum in each group.
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292 **Table 2.** Psychological general well-being (PGWBI) global score and subscales in late pregnancy and three months postpartum. “Intention to treat”
 293 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					
		Score at baseline N = 91	Score late pregnancy N = 38	Score postpartum N = 36	Score late pregnancy N = 36	Score postpartum N = 34	Late pregnancy			Postpartum	
						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

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

296 We found no statistically significant difference in total EPDS score three months postpartum
297 between the exercise group (2.96, 95% CI 1.7, 4.2) and the control group (3.48, 95% CI 2.3,
298 4.7) ($p = 0.55$). None reported of a total EPDS score of 13 or more, representing indication of
299 major depression. Two women (7.1%) in the exercise group and three women (10.3%) in the
300 control group reported at total EPDS score between 10 and 12, representing indication of a
301 minor depression. In the per-protocol analysis, there was no statistical significant difference in
302 total EPDS score between the exercise group (2.38, 95% CI 1.72, 4.2) and the control group
303 (3.48, 95% CI 2.3, 4.7) ($p = 0.30$).

304 **Baseline comparison within the exercise group**

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

308 **Harms**

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

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314 **Discussion**

315 **Main findings**

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

327 **Strengths and weaknesses of the study**

328 The major strength of this study was the randomised controlled design. We assessed well-being
329 by valid and reliable questionnaires.^{55,56} We included only women with pre-pregnancy
330 overweight and obesity (BMI \geq 28 kg/m²) in the trial, contributing to a homogenous study
331 group. We recorded exercise adherence as well as self-reported physical activity levels
332 throughout the trial period in both groups.

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

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3 338 These factors limit the chance of estimating a true effect of exercise training on psychological
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5 339 well-being. Furthermore, the relatively high level of physical activity in the control group could
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7 340 have reduced the chance of finding an effect of the intervention. Our trial included
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9 341 comprehensive health assessments and close monitoring of the women, regardless of group
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11 342 allocation. This close follow-up by health personnel may have prevented reduced psychological
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13 343 well-being among all the women in the trial. We had no information on previous mental health
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15 344 history or use of antidepressant treatment among the participants.
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20 345 **Comparison with other trials**

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22 346 Observational studies show that women who are physically active during pregnancy report
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24 347 better psychological well-being than less active women²⁸ and that the risk of psychological
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26 348 health problems increases in parallel to decreased frequency of exercise during pregnancy.²⁷ A
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28 349 limited number of RCTs have investigated the effects of exercise training in pregnancy on
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30 350 psychological well-being, and the results diverge.^{29,30,57} Bogaerts and colleagues³⁰ showed
31
32 351 reduced anxiety in late pregnancy among obese women who received an intervention
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34 352 combining regular motivational interviewing with advice about healthy eating and physical
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36 353 activity in pregnancy, compared to advice only or a standard care control group. They found no
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38 354 effect of the intervention on depression.³⁰ In our study, the level of anxiety did not differ
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40 355 between groups in late pregnancy, but we observed a tendency of less symptoms of anxiety
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42 356 among the women who adhered to the exercise program compared to the control group, which
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44 357 indicates a positive effect of regular exercise during pregnancy on the risk of anxiety.
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46 358 Gustafsson and co-workers²⁹ investigated the effect of regular exercise during pregnancy on
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48 359 late pregnancy psychological well-being using PGWBI. They included women in all BMI
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50 360 categories, and found, similar to our trial, no effect of exercise on mental health. Also in their
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52 361 trial, the participants reported of good psychological well-being at baseline. This is in contrast
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54 362 to previous studies showing a high prevalence (15-25%) of depression and anxiety among
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3 363 overweight and obese pregnant women^{2,7,8,58-61} and that especially the levels of anxiety
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5 364 increases from early to late pregnancy in this population.⁵⁹ Compared to the general population
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7 365 of pregnant women with overweight/obesity, a higher percentage of women in the ETIP trial
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9 366 reported to fulfil the recommendations for physical activity during and after pregnancy³², the
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11 367 number of pregnancy complications were lower, as was the percentage of women exceeding
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13 368 the Institute of Medicine guidelines for gestational weight gain.^{32,33} Low level of physical
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15 369 activity and exceeding the recommended gestational weight gain are both associated with
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17 370 increased risk for reduced psychological well-being, and these factors could therefore explain
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19 371 stable PGWBI scores during pregnancy in our study group. Again, this indicates that we
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21 372 included women with good psychological well-being in our trial.
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26 373 We found no effect of exercise training on the risk for postnatal depression, which is in
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28 374 line with previous studies suggesting limited effect of exercise interventions during pregnancy
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30 375 on risk for depression after delivery.^{31,57} Few of the participating women reported symptoms
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32 376 of postnatal depression in our trial. This is in contrast to a systematic review and meta-analysis
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34 377 reporting a high risk of developing depression during the postpartum period for women with
35
36 378 pre-pregnancy obesity.¹ Also a cohort study by Ertel and colleagues,⁵ who assessed postnatal
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38 379 depression among 1686 women in all BMI categories, found that pre-pregnancy BMI >30 was
39
40 380 associated with increased risk for depression six months postpartum. The EDPS records the
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42 381 woman's self-perceived psychological well-being during the last week, and thereby the
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44 382 woman's current state of anxiety and depression. On the other hand, the "State and Trait
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46 383 Anxiety Inventory (STAI)" questionnaire, assesses both short-term and long-term symptoms,
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48 384 and might provide a different set of information compared to the EDPS. Even though the EDPS
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50 385 is the most frequently used questionnaire for assessing risk for depression postpartum, the use
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52 386 of different questionnaires in comparative trials hampers comparison between studies.
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58 387 **Generalizability and clinical implications**

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3 388 When compared to women in the Norwegian Medical Birth Registry,⁶² the ETIP participants
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5 389 are representative for Norwegian pregnant women with overweight/obesity, according to BMI,
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7 390 obesity grades I, II, III, age, education, parity and occupational activity/employment.³²
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9 391 However, it is likely that women who volunteer for participation in an exercise trial are extra
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11 392 aware of possible benefits of maternal exercise, are more experienced with physical activity
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13 393 and suffer from less pregnancy complications. We believe that the findings of our study can be
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15 394 generalized to relatively healthy pregnant women with pre-pregnancy BMI of 28 or more.
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19 395 We based the trial intervention program on current recommendations for maternal
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21 396 exercise and designed it for easy implementation into clinical practice. Health care
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23 397 professionals, especially general practitioners and midwives who consult pregnant women, are
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25 398 in a unique position to inform, help and guide women with high BMI throughout pregnancy.
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27 399 Distinct recommendations for exercise and physical activity should be given to all pregnant
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29 400 women, and the women should be closely monitored and motivated by maternal health care
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31 401 personnel throughout pregnancy. Assessing psychological well-being early in pregnancy may
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33 402 be important for prediction of adherence to exercise during pregnancy.
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38 403 **Conclusion**

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40 404 We found no statistically significant effects of supervised exercise training during pregnancy
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42 405 on psychological well-being in late pregnancy or postpartum, nor on the prevalence of
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44 406 symptoms of postnatal depression, among women with overweight or obesity. Both the exercise
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46 407 group and the control group reported good psychological well-being and low risk for postnatal
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48 408 depression. The level of self-control early in pregnancy may be important for exercise
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50 409 adherence during pregnancy. Low adherence to the exercise protocol in our trial could have
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52 410 reduced the chance of finding an effect of regular maternal exercise on mental health.
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3 411 We need adequately powered trials, with good adherence to the intervention protocol, to be able
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5 412 to investigate the true effect of exercise during pregnancy on maternal well-being and to
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7 413 examine factors associated with motivation for exercise during pregnancy.
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11
12
13 423 women received infant food from Nestlé worth 500 Norwegian kroner.
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19 425 **Data sharing statement:** Extra data can be accessed via the Dryad data repository at
20
21 426 <http://datadryad.org/> with the doi: 10.5061/dryad.pvmcvdng6
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25 427 **Author Contributions:** KKG acquired the data, analysed the data, interpreted the data and
26
27 428 drafted the manuscript. ASH interpreted the data and critically revised the manuscript. SM
28
29 429 designed the study and critically revised the manuscript, SNS designed the study and critically
30
31 430 revised the manuscript, KÅS designed the study and critically revised the manuscript, ØS
32
33 431 provided the statistics in previous published papers in the ETIP trial, and reviewed statistical
34
35 432 methods in the current manuscript, TM acquired some of the data, deigned the study and
36
37 433 critically revised the manuscript. All authors have approved the final version of the manuscript
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40 434 and are accountable for all aspects of the work.
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6 609 **Figure 1.** CONSORT flow chart ETIP trial.
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10 611 **Figure 2.** Changes in the Psychological General Well-Being Index (PGWBI) global score and
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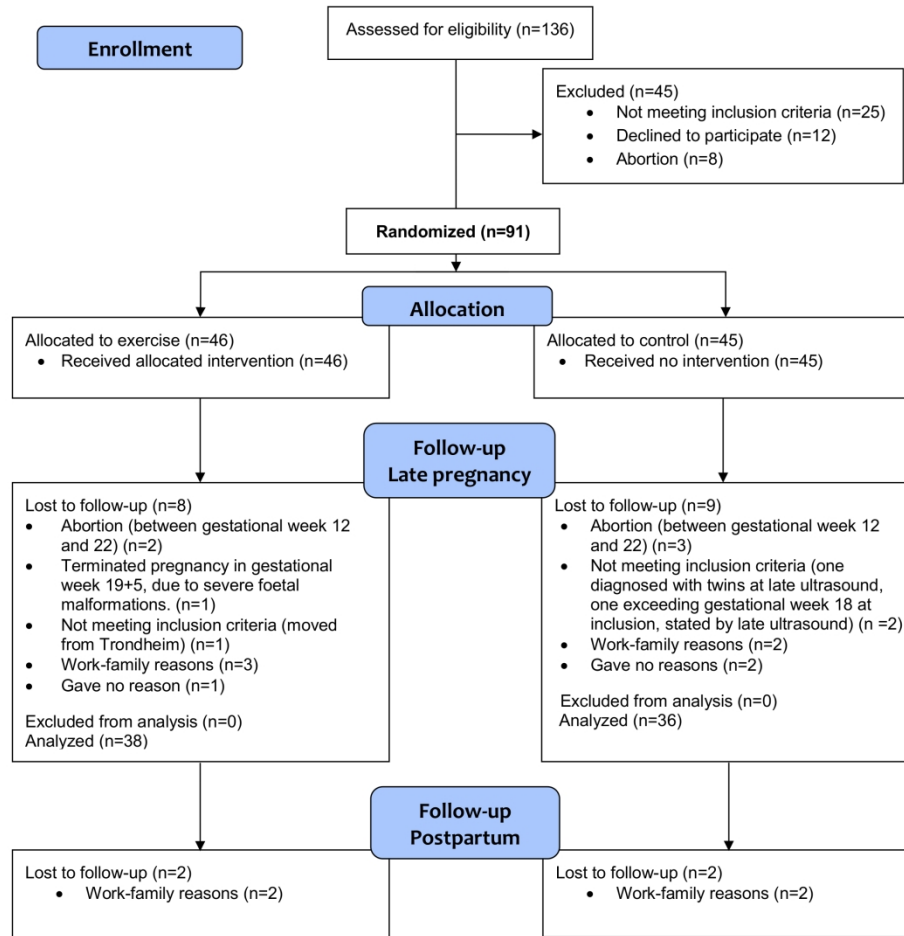
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20 615 **Figure 3.** Changes in the Psychological General Well-Being Index (PGWBI) global score and
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CONSORT Flow Diagram



CONSORT Flow chart ETIP trial

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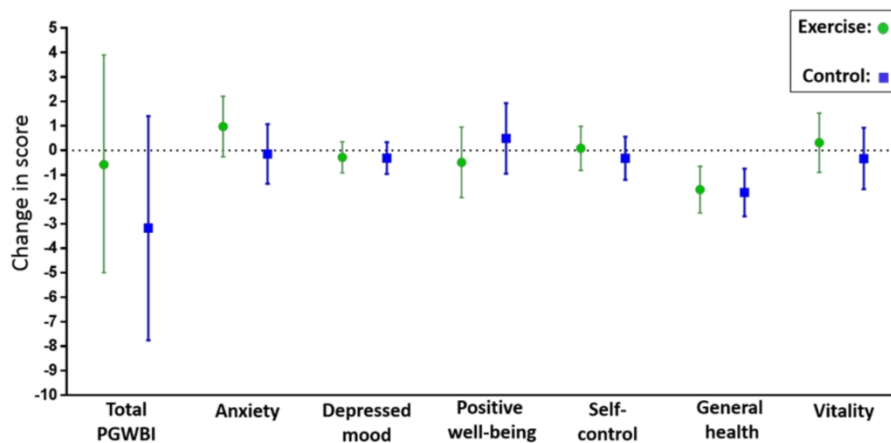


Figure 2. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from baseline to late pregnancy in the exercise group and the control group. Data are means with 95% confidence intervals.

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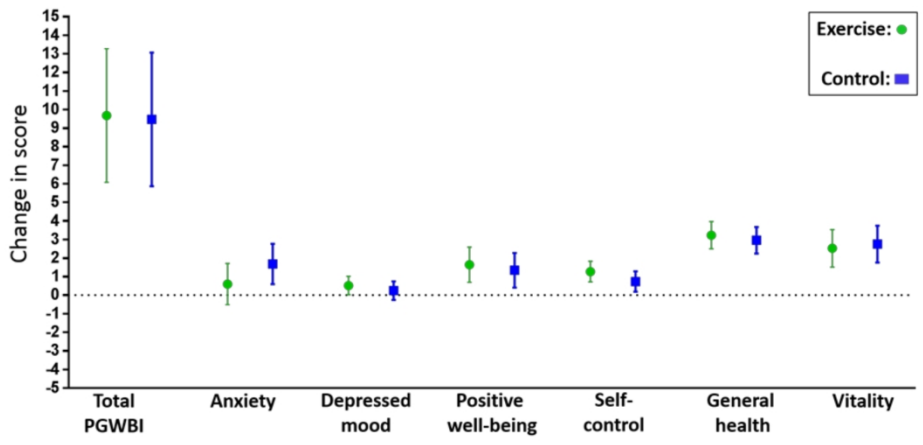


Figure 3. Changes in the Psychological General Well-Being Index (PGWBI) global score and the six subscales from late pregnancy to postpartum in the exercise group and the control group. Data are means with 95% confidence intervals.

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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					
	Score late pregnancy <i>N</i> = 19	Score postpartum <i>N</i> = 19	Score late pregnancy <i>N</i> = 36	Score postpartum <i>N</i> = 34	Late pregnancy			Postpartum		
					<i>Diff</i>	<i>95% CI</i>	<i>P-value</i>	<i>Diff</i>	<i>95% CI</i>	<i>P-value</i>
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
<p><i>Missing late pregnancy:</i> Exercise 6, control, 5. <i>Missing postpartum:</i> Exercise 5, control 4.</p> <p><i>Statistics:</i> 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.</p> <p>PGWBI: The Psychological General Well-Being Index (global score of all subscales).</p>										

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 Salvesen², Charlotte B Ingul³, Torstein Vik⁴, Emily Oken⁵ and Siv Mørkved¹

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/m².

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/m². 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 United States over one-third of reproductive age women are obese (body mass index (BMI) ≥ 30 kg/m²) and another 29% are overweight (BMI 25.0-29.9 kg/m²) [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/m² 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.

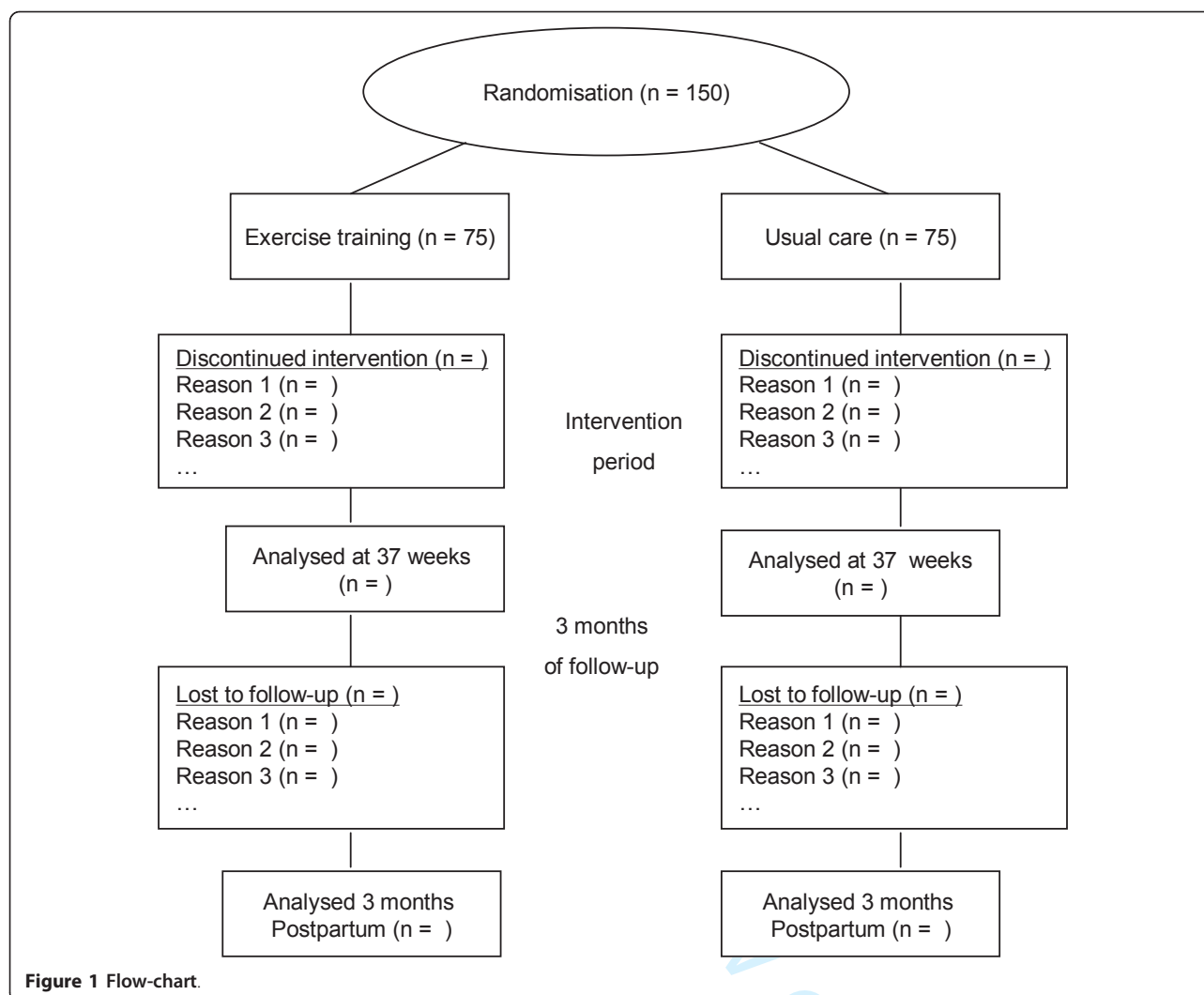
The trial will be conducted at the Norwegian University of Science and Technology and the St.Olavs Hospital, Trondheim University Hospital. The recruitment started in September 2010 and will continue until the needed number of participants is included, anticipated until the end of 2012. Participating 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



maximal capacity in periods (corresponding to Borg scale 12-15) [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 as 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

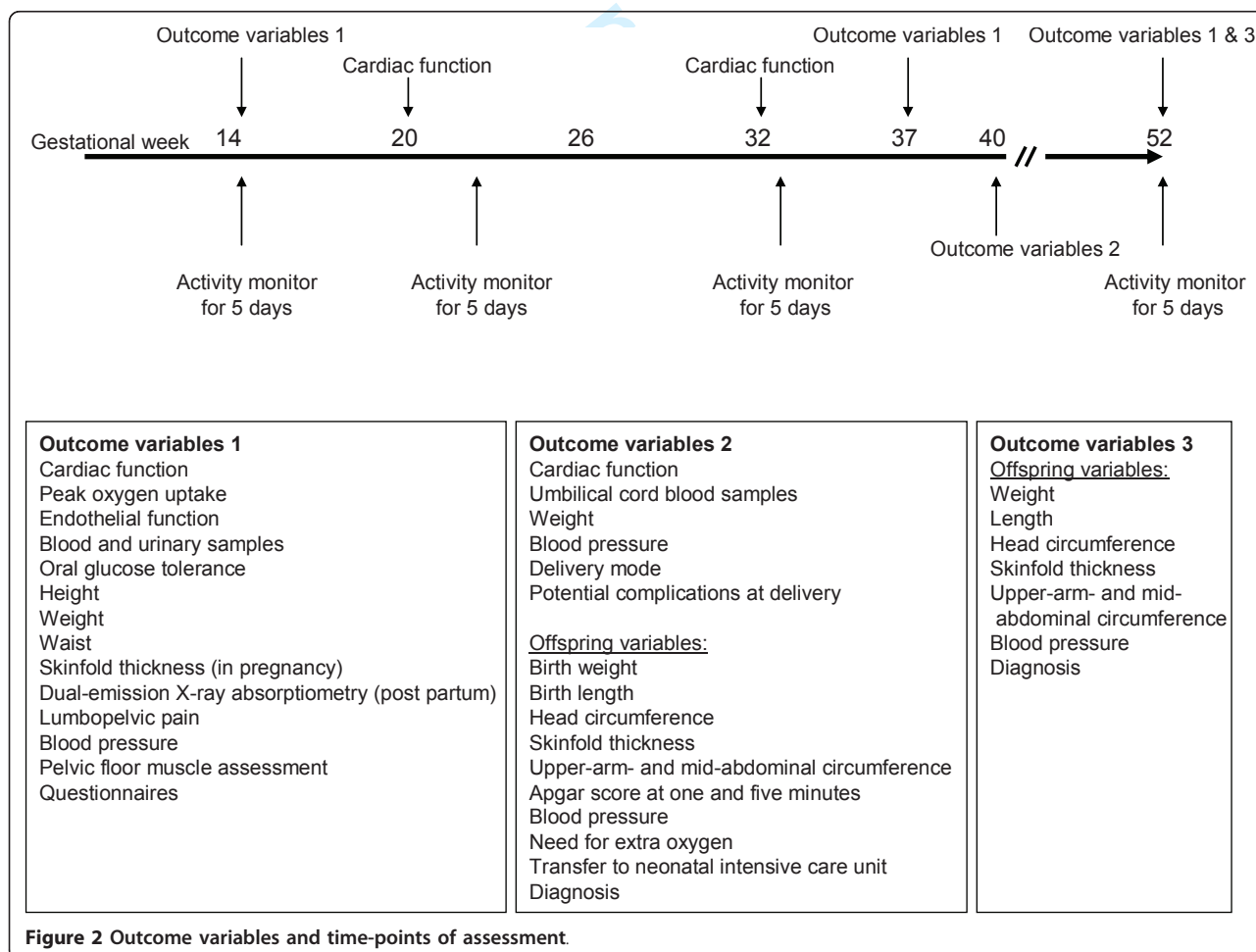
The primary outcome measure is gestational weight gain, calculated as the difference between weight measured at the time of inclusion and weight just before delivery. We measure maternal body weight at enrolment and before delivery to the nearest 0.1 kg with a calibrated electronic scale (SECA 770, Medema, 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



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 urinary samples 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 an 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 Gynecologica Scandinavica*). 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]. Neuro-motor 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

TM participated 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. CBI participated in conceiving and designing the study and in critically revising the manuscript, as well as approving the final version to be published. TV participated in conceiving and designing the study and in critically revising the manuscript, as well as approving the final version to be published. EO participated in conceiving and designing the study and in critically revising the manuscript, as well as approving the final version to be published. SM participated in conceiving and designing the study and in

critically revising the manuscript, as well as approving the final version to be published

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

1		assessing outcomes) and how	
2	11b	If relevant, description of the similarity of interventions	
3	Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes
4		12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses
5			
6	Results		
7	Participant flow (a	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and
8	diagram is strongly		were analysed for the primary outcome
9	recommended)	13b	For each group, losses and exclusions after randomisation, together with reasons
10	Recruitment	14a	Dates defining the periods of recruitment and follow-up
11		14b	Why the trial ended or was stopped
12	Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
13	Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was
14			by original assigned groups
15			
16	Outcomes and	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its
17	estimation		precision (such as 95% confidence interval)
18		17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
19	Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing
20			pre-specified from exploratory
21	Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)
22			
23	Discussion		
24	Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
25	Generalisability	21	Generalisability (external validity, applicability) of the trial findings
26	Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
27			
28	Other information		
29	Registration	23	Registration number and name of trial registry
30	Protocol	24	Where the full trial protocol can be accessed, if available
31	Funding	25	Sources of funding and other support (such as supply of drugs), role of funders
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*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.