Effect of supervised group Exercise on psychological WEll-being among pregnant women with or at high risk of depression (the EWE Study): a randomised controlled trial

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Abstract

Objective To assess the effect of supervised group exercise on psychological well-being and symptoms of depression among pregnant women with or at high risk of depression. Design Randomised, controlled trial. Setting Department of Obstetrics, Copenhagen University Hospital, Rigshospitalet, Denmark. Population Pregnant women with a current or previous history of depression or/and anxiety requiring treatment within the last ten years, or use of antidepressants three months prior to or during pregnancy. Methods From August 2016–September 2018 the participants were randomly assigned to 12 weeks supervised group exercise from 17–22 weeks of gestation twice weekly, or to a control group. Main outcome measures The primary outcome was self-reported psychological well-being at 29–34 weeks of gestation, measured by the five-item World Health Organization Well-being Index (WHO-5). Secondary outcomes included delivery outcomes and psychological well-being (WHO-5) eight weeks postpartum. Results The analysis showed no significant effect on psychological well-being on the primary outcome. Mean WHO-5 score in the intervention group was 2.0 (95% CI: –1.3 to 5.2, p=0.2) higher than in the control group. Eight weeks postpartum the intervention group reported higher psychological well-being than the control group, mean difference in WHO-5 of 5.5 (95% CI: 1.0–10.1, p=0.04). Conclusions Supervised group exercise did not improve psychological well-being for women with or at high risk of depression at 29–34 weeks of gestation. Eight weeks postpartum the intervention group reported significant higher psychological well-being than the control group. Funding The Danish foundation TrygFonden and Copenhagen University Hospital, Rigshospitalet. ClinicalTrials.gov (NCT02833519). https://clinicaltrials.gov/ct2/show/NCT02833519?term=EWE&cntry=DK&draw=2&rank=1

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Abstract

Objective

To assess the effect of supervised group exercise on psychological well-being and symptoms of depression among pregnant women with or at high risk of depression.

Design

Randomised, controlled trial.

Setting

Department of Obstetrics, Copenhagen University Hospital, Rigshospitalet, Denmark.

Population

Pregnant women with a current or previous history of depression or/and anxiety requiring treatment within the last ten years, or use of antidepressants three months prior to or during pregnancy.

Methods

From August 2016–September 2018 the participants were randomly assigned to 12 weeks supervised group exercise from 17–22 weeks of gestation twice weekly, or to a control group.

Main outcome measures

The primary outcome was self-reported psychological well-being at 29–34 weeks of gestation, measured by the five-item World Health Organization Well-being Index (WHO-5). Secondary outcomes included delivery outcomes and psychological well-being (WHO-5) eight weeks postpartum.

Results

The analysis showed no significant effect on psychological well-being on the primary outcome. Mean WHO-5 score in the intervention group was 2.0 (95% CI: –1.3 to 5.2, p=0.2) higher than in the control group. Eight weeks postpartum the intervention group reported higher psychological well-being than the control group, mean difference in WHO-5 of 5.5 (95% CI: 1.0 –0.1, p=0.04).

Conclusions

Supervised group exercise did not improve psychological well-being for women with or at high risk of depression at 29–34 weeks of gestation. Eight weeks postpartum the intervention group reported significant higher psychological well-being than the control group.

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Introduction

Depression is expected to be the leading cause of disability worldwide by 2030 (1). The prevalence is increasing, women being particular at high risk during hormonal transition phases such as pregnancy and the postpartum period (2,3). Systematic reviews report an 12% prevalence of depression antenatally (4) and 19% in the first three months postpartum (5). Antenatal depression is associated with preterm birth, a lower likelihood of initiating breastfeeding, and postpartum depression (6). Both antenatal and postpartum depression are associated with compromised mother-infant bonding, and with adverse effects on later childhood development i.e. attention- and hyperactivity problems (7–9). A previous history of mental illness, in particular depression and anxiety are strongly associated with antenatal (10) and postpartum depression (11).

This public health challenge have led to national and international guidelines recommending a coordinated care plan for pregnant women with a current or a history of mental health disorders (12,13), including psychosocial support and, in more severe cases, antidepressant medication (13,14). Outside pregnancy exercise has shown a positive effect among clinically depressed men and women (15), and interestingly, pregnant women with clinical depression expressed interest in exercise as part of their care (16). In a systematic review from 2014, the authors found that exercise might be effective in treating antenatal depression (17). This was based on six randomised controlled trials (RCTs) with small samples sizes (n=24–92) where adherence to physical intervention was not reported in four studies. Further, it was unclear if treatment allocation was concealed properly and intention-to-treat analysis was not conducted in any of the studies (17). We found that the effect of exercise on self-reported psychological well-being among pregnant women with or at high risk of depression needed to be further investigated and undertook a large randomised controlled trial.

Objective

Our objective was to assess the effect of supervised group exercise on psychological well-being and symptoms of depression among pregnant women with or at high risk of depression

Methods

Study design

This study, labelled the EWE Study, was designed as a randomised, controlled parallel-group trial with a 1:1 allocation ratio. Participants were randomised from August 2016–September 2018 at Copenhagen University Hospital, Rigshospitalet, Denmark, with follow-up until April 2019. The hospital is a tertiary referral center with 5,406 deliveries in 2018 and serves as a primary birth facility for residents of Copenhagen.

The EWE Study was designed in accordance with the Consolidated Standards of Reporting Trials (CONSORT) (18). The Ethics Committee of the capital region of Denmark (Journal no.: H-15019905) and the Danish Data Protection Agency (Journal no.: 2012-58-0004) approved the study. The study was registered at ClinicalTrials.gov (NCT02833519), and a detailed study protocol has been published (19).

Participants

Participants were recruited at 12–14 weeks of gestation among pregnant women attending antenatal care at the Department of Obstetrics, Rigshospitalet. Pregnant women were eligible to participate if they had depression and/or anxiety requiring treatment by a psychiatrist, general practitioner or a psychologist within the previous ten years, and/or if they used antidepressants in the three months prior to or during pregnancy. Depression and anxiety was defined according to The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria (20).

The participants meet the following inclusion criteria: [?]18 years of age, appropriate Danish language skills, singleton pregnancy, and at 17–22 gestational weeks at the start of the intervention. Women fulfilling these criteria but with a chronic disease were only included in the study after prior agreement with their obstetrician. Participants were withdrawn from the intervention after randomisation for the following reasons: development of pelvic girdle syndrome, preeclampsia, vaginal bleeding, or symptoms of preterm labour contraindicating physical activity (19).

Procedures

Pregnant women with a current or previous history of depression and/or anxiety who were interested in participating were invited to a face-to-face visit with a research midwife (19). All participants provided written informed consent and completed a self-administered electronic baseline questionnaire. All baseline data were collected before randomisation.

Randomisation

The participants were randomly assigned to either the intervention group or the control group (ratio 1:1) at baseline by a computer-generated random sequence, using random permuted block randomisation sizes (four, six or eight). Proper concealment was accomplished through the use of external randomisation service (Clinical Trial Unit, Department of Clinical Medicine, Aarhus University, Denmark). Each participant's Central Personal Register (CPR) number was entered in the computer program (Trialpartner) by a research midwife, and thereby each participant was allocated to a group. The researchers were involved in inclusion of the participants and while the intervention consisted of exercise, neither participants nor researchers were blinded to group allocation after the randomisation procedure. The statistician performing the analyses were not blinded to the group allocation due to the prespecified perprotocol analysis.

Intervention group

From 17–22 gestational weeks, the intervention group was offered supervised group exercise twice a week for 12 weeks at the training centre at the Rigshospitalet Clinic of Occupational Therapy and Physiotherapy. The exercise intervention was developed and supervised by four physiotherapists from Rigshospitalet in accordance with the Danish national recommendations for exercise during pregnancy (21). The intervention is described in details in the study protocol (19).

To increase compliance, a weekly supportive email was sent to the participants in the intervention group and the women's general practitioners were informed about the intervention. Participation was recorded by the physiotherapists at each session as a standard procedure.

Control group

The control group as well as the intervention group were offered usual antenatal care for pregnant women with a current or a previous history of depression or anxiety; all received care at the Department of Obstetrics, Rigshospitalet. This care is free of charge and covers a coordinated program including lengthier and more frequent prenatal visits with specialised midwives and obstetricians experienced with pregnancy and mental health disorders. These visits include guidance on physical exercise for pregnant women (at least 30 min of moderate intensity per day unless physical activity is contraindicated).

Patient Involvement

When designing the intervention regimen, five pregnant women from the target population were asked about preferred group size, duration of exercise sessions and whether there should be separate time for socialising after each session. This patient involvement led to minor changes before the pilot study was initiated (19).

Prespecified outcomes

Participants received a link to the self-administered questionnaires by email at 29–34 weeks of gestation and eight weeks postpartum. Thereafter, additional outcome indicators were gathered from medical records.

Primary outcome

The primary outcome was self-reported Psychological well-being at 29–34 weeks of gestation by the five-item World Health Organization Well-being Index (WHO-5). The WHO-5 measures current, general, subjective psychological well-being covering the prior two weeks, and consists of five items, each scored on a Likert scale (from 0 = "none of the time" to 5 = "all of the time"). Because scales measuring health-related quality of life are usually translated to a percentage scale from 0 (lowest possible well-being) to 100 (highest possible well-being), the raw WHO-5 ranging from 0 to 25 were multiplied by a factor of 4. Using a cut-off score of [?]50 the WHO-5 has a high sensitivity (0.87) and specificity (0.76) for depression defined according to the DSM- IV (22).

Secondary outcomes

The secondary outcomes are described in details in the study protocol (19).

The following secondary outcomes were self-reported:

Psychological well-being, measured by WHO-5 eight weeks postpartum. In the planning of the trial this secondary was the highest prioritised secondary outcome (19). The remaining secondary outcomes were not ranked.Functional ability, measured by General Health Questionnaire (GHQ-12), clinical symptoms of anxiety, measured by the Spielberger State-Trait Anxiety Inventory (STAI), symptoms of depression defined as a cut-off score of [?]11 on the Edinburgh Postnatal Depression Scale (EPDS) were all measured 29–34 weeks of gestation and eight weeks postpartum. Based on a resent Danish study validating the Danish version of the EPDS against a diagnosis of depression in a sample of new mothers, we changed our predefined cut-off scores of [?]10 and [?]13 on the EPDS to a cut-off score of [?]11 (23). Further self-reported secondary outcomes were exclusive breastfeeding at eight weeks postpartum and sick leave in days from intervention start until labour.

The following secondary outcomes were obtained from medical records:

Preeclampsia, gestational age (days) at delivery, preterm delivery (> three weeks before term), induction of labour, mode of delivery (spontaneous delivery, instrumental delivery, or caesarean section), epidural anesthesia during delivery, duration of labour (hours), birth weight (gram), birth length (centimeters), Apgar

score (<7 at 5 min), arterial pH (<7.10), antenatal contacts (number), antenatal telephone consultations (number), and length of hospital stay (days).

All secondary outcomes are describes in details in the study protocol (19).

Statistical analysis

The sample size calculation has previously been described in detail (19). At 29–34 weeks of gestations we expected a mean difference of 7.75 (SD=16) in WHO-5 between the intervention group and the control group. Based on a two-sample t-test and a two-sided significance level of 0.05, 91 women are required in each treatment group to obtain a power of 90%. A total of 300 women were planned to be randomised allowing for a 13% drop out as a result of discomfort or complications and a further 30% drop out due to refusal to fill in the questionnaires.

To account for missing values under the assumption of Missing At Random (MAR) and to adjust for potential baseline imbalances between the two treatment groups, quantitative outcomes were analysed using constrained linear mixed models considering scores measured baseline, 29–34 weeks of gestation and eight weeks postpartum as outcomes (24). The fixed part of the models included the interaction between group (intervention and control) and time (baseline/29–34 weeks/eight weeks postpartum) with the constraint that the means in the two groups were assumed equal at baseline due to randomisation. The random part of the model included a random intercept for each patient.

For each group and each time point, the proportion of women with EPDS [?]11 was estimated from a logistic regression model with parameters estimated by weighted Generalised Estimating Equations (GEE) to account for repeated measures and missing data (25). The weights were defined as the inverse probabilities of being observed conditional on previous measurements of EPDS (quantitative), treatment group and previous missing value of EPDS and were estimated from a logistic regression model. An unstructured correlation matrix was used as the working correlation.

As specified in the protocol (19), analysis of WHO-5 was repeated based on the sub group of women attending [?]75% of the sessions. In this analysis, the linear mixed model was not constrained to assume equal means at baseline as the randomisation is not valid for this group of women.

Due to the large number of hypotheses tested, correction for multiple testing was applied. The p-value corresponding to the comparison of the secondary outcome (WHO-5 at eight weeks postpartum) was adjusted accounting for the test of the primary outcome, there by multiplying the p-value by 2 (False Discovery Rate method). The remaining secondary outcomes are presented uncorrected for multiple testning.

Results

Trial participants

From August 2016–September 2018, 714 pregnant women were assessed for eligibility. A total of 67 women did not receive information about the study and 647 were initially invited to participate. A total of 282 women were randomly assigned to either supervised group exercise (n=143) or the control group (n=139) (Figure 1). Eight women from the intervention group withdrew consent: one found the exercise uncomfortable to perform, two preferred other kinds of physical activity and five women could not find the time to participate.

Baseline maternal characteristics in the intervention group and the control group were comparable (Table 1).

The study population's mean age was 31.8 years (SD 3.9), 73.4% were nulliparous, the mean pre-pregnancy body mass index was 22.8 kg/m^2 (SD 3.5), 87% had a higher education or advanced degree, 99% did not smoke at baseline and 78% of the study population were physically active [?]3.5 hours a week before pregnancy. The median weekly amount of physical activity was measured after the intervention and eight weeks postpartum: 4 hours (min 0–max 24) in the intervention group and 4 hours (min 0–max 16) in the

control group at 29–34 weeks of gestation, 6 hours (min 0–max 25) in the intervention group and 6 hours (min 0–max 25) in the control group eight weeks postpartum.

A total of 127 (95%) participants in the intervention group and 118 (86%) in the control group responded to the self-administered questionnaire at 29–34 weeks of gestation, while 99 (74%) participants in the intervention group and 84 (61%) in the control group responded eight weeks postpartum (Figure 1).

Primary outcome

The intervention was completed as planned. Adherence to the intervention was as follows: 55 (42%) participants attended [?]75% of the exercise sessions, 47 (35%) attended 50–74% of the sessions, and 31 (23%) attended fewer than half of the exercise sessions.

We found no effect of supervised group exercise on psychological well-being measured by the WHO-5 at gestational week 29–34. The mean WHO-5 score was 60.5 (95% CI: 58.1–63.0) in the intervention group and 58.5 (95% CI: 56.0–61.1) in the control group, mean difference between the two groups being 2.0 (95% CI: -1.3 to 5.2, p=0.23) (Table 2).

The prespecified perprotocol analysis of women attending [?]75% of the exercise sessions showed a statistically significant higher WHO-5 mean score in the intervention subgroup compared to the control group at gestational week 29–34, mean difference 5.5 (95% CI: 0.8-10.2, p=0.02).

Predefined secondary outcomes

Eight weeks postpartum, a mean difference of 5.5 (95% CI: 1.0–10.1) p=0.04 (corrected for multiple testing) in WHO-5 score between the intervention and the control group was seen, the mean WHO-5 score being 60.2 (95% CI: 57.1–63.3) in the intervention group and 54.7 (95% CI: 51.3–58.1) in the control group (Table 2).

No difference was found in maternal or infant outcomes (Table 3) except for induction of labour where 27.2% in the control group versus 15.8% in the intervention group had their labour induced, p=0.02. There was no difference with regards to the medical indications for induction in the two groups (data not shown). The groups also did not differ with regards to sick leave, contacts to the hospital, or length of hospital stay (Table 4). Finally, no major adverse effects or health problems resulting from the exercise intervention were reported.

Discussion

Main findings

In this large RCT, the intention-to-treat analysis showed no effect of a supervised 12 weeks group exercise intervention on psychological well-being measured by the WHO-5 at gestational weeks 29–34 (primary outcome). Perprotocol analysis of women who attended [?]75% of the exercise sessions showed a statistically significant higher WHO-5 mean relative to controls at gestational weeks 29–34. Intriguingly, eight weeks postpartum, women in the intervention group had a statistically significant higher mean WHO-5 than women in the control group.

Strengths and limitations

This RCT is to the best of our knowledge the largest study in this field. Compliance with the intervention was registered by the physiotherapists to ensure accuracy of the data and this is also considered a strength. The degree of exertion during exercise sessions was subjectively measured using The Borg Scale of Percived Exertion (26). The use of accelerometers would have made it possible to objectively determine the actual time and intensity (27). It is a strength that WHO-5 is a simple, validated patient-reported outcome measure, used as an outcome in the obstetric field (22), although not validated in a population of pregnant women. The generalisability of the trial results is limited due to a selected population of women at high risk for perinatal depression where the participants were highly educated, had a high level of physical activity before, during and after pregnancy, had normal BMIs, and understood the Danish language. It might be seen as a limitation that a large proportion of eligible women declined to participate. Based on the legislation, The

Ethics Committee of the capital region of Denmark could not to let us describe the characteristics of those who declined to participate. We cannot rule out that there is a greater proportion of multi parous among the women who declined to participate. In this study population approximately 25% was multi parous, and in the population of pregnant women referred to Rigshospitalet, the proportion of multi parous is approximately 40%. One of the inclusion criteria was depression and/or anxiety requiring treatment by a psychiatrist, general practitioner or a psychologist within the last ten years before pregnancy. This information was self-reported, which is considered a strength in the context, since mild to moderate mental disorders are often diagnosed and treated outside primary care and thus not registered in the medical records nor in The Danish Psychiatric Central Research Register (28). To strengthen the validity of self-reported diagnoses, the pregnant women were asked to elaborate on the circumstances related to the diagnosis, including symptoms and treatment, when contacted by telephone by a specialised midwife.

Interpretation

We found no difference in psychological well-being at 29–34 weeks of gestation between the intervention group and the control group. In contrast a systematic review from 2018 concluded that prenatal exercise reduces the odds and the severity of prenatal depressive symptoms (29). The authors included thirteen studies (n=1,076) in the analysis, seven of these had a population at risk of or currently diagnosed with depression (29). Our result might be explained by a comparable level of general physical activity at 29–34 weeks of gestation in both the intervention and the control group, median physical activity being 4 hours (min 0–max 24) in the intervention group and 4 hours (min 0–max 16) in the control group. This indicates that the intervention did not help women to increase their physical activity rather just changed the physical activity behavior, which may be explained by the womens high level of physical activity preconceptionel in this study population (30). The perprotocol analysis of women attending [?]75% of the exercise sessions showed a statistically significant higher WHO-5 mean in the intervention subgroup relative to the control group (29). While we, based on the literature (22), predefined a mean difference between the two groups of minimum 7.75 point as clinically significant (19). Further, this is a selected subgroup and therefore it is not possible to draw conclusions from our perprotocol analysis as it can be flawed (31).

At eight weeks postpartum, women in the intervention group had a statistically significant higher mean WHO-5 than women in the control group signifying a greater level of psychological well-being. In line with our result, a systematic review found that physical activity during pregnancy reduced the risk of postpartum depressive symptoms, however, in a population of women at average risk for depression (32). In contrast, Davenport (29) found that exercise during pregnancy did not have an effect on postpartum psychological well-being, however the exercise interventions were primarily homebased exercise. Our positive results postpartum may be explained by psychosocial factors such as increased perceived peer-support and reduced loneliness, as previously reported for women in the intervention group (33). This is in line with other studies which imply that peer support may reduce the risk of postpartum depression by enabling sharing of experiences, reassurance that other mothers experience similar feelings, and a sense of belonging (34,35).

Regarding maternal delivery outcomes we did not conform our hypothesis that the intervention group would have a significant shorter duration of labour (36). This may be due to a high level of physicial activity in the control group. An interesting finding was that only 15.8% of women in the intervention group had labor induced, opposed to 27.2% in the control group. Although this is in line with findings from a prospective cohort study (37) and a non-randomised intervention study (38), it may represent a spurious finding and we interpret this with caution.

Conclusion

Supervised group exercise did not improve psychological well-being at 29–34 weeks of gestation among pregnant women with depression or at high risk of depression. Eight weeks postpartum women in the intervention group had a higher mean WHO-5 than women in the control group, which may be due to the exercise itself but also due to the participants' experience of peer support. Based on our results, supervised exercise in groups is a safe complementary course of treatment alongside the existing antenatal care. Further

studies are needed to explore the effect of supervised group exercise among sedentary pregnant women with or at high risk of depression.

Abbreviations

CI: Confidence Interval; CONSORT: Consolidated Standards of Reporting Trials; DSM-IV: The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DSM-V: The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; EPDS: Edinburgh Postnatal Depression Scale ; GHQ-12: General Health Questionnaire; P value: probability value; RCT: randomised controlled trial; SD: standard deviation; STAI: The Spielberger State Trait Anxiety Inventory; WHO-5: The five-item World Health Organization Well-being Index.

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Consent for publication

Not applicable.

Disclosure of Interests

None declared. Full disclosure of interest available to view online as supporting information.

Contribution to authorship

All authors met all four criteria for authorship in the ICMJE Recommendations. HKH is the principal investigator of the EWE Study. HKH designed the trial and coordinated the main preparation of study documents and the funding application. LB, PD, AT, MB and HKH contributed to the funding application and the study design. VGF provided important expertise regarding psychometry and supported analysis structure and interpretation. SR did the data analysis. LB was responsible for the data collection and drafted the first draft of the manuscript. All authors have read, reviewed and approved the final version of this manuscript.

Details of Ethics approval

The Danish Data Protection Agency (journal no.: 2012-58-0004) and the Ethics Committee of the capital region of Denmark approved the trial protocol (journal no.: H-15019905, date of approval February 26, 2016), which qualified for registration in the ClinicalTrials.gov (number identifier: NCT02833519).

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Table Caption List

Table 1. Baseline data, characteristics of the study participants, N= 282

Table 2. Assessment of psychological well-being

Table 3. Maternal and infant outcomes

Table 4. Economical outcomes

Table 1

Characteristics	**Intervention group n=143**	**Control group n=139**
Maternal age (years), mean (SD)	31.9 (3.8)	31.7 (3.9)
Body mass index (kg/m^2), mean (SD)	22.8 (3.4)	22.7 (3.6)
Nulliparous, n (%)	107 (74.8)	100 (71.9)
Living with partner, n (%)	137 (95.8)	132 (95.0)
Educational level, n (%)		
Advanced degree	72 (50.3)	74 (53.2)
3–4 years higher education	47 (32.9)	40 (28.8)
1–2 years higher education	9 (6.3)	5 (3.6)

Table 1

Skilled worker	4 (2.8)	8 (5.8)
Compulsory education	11 (7.7)	10 (7.2)
Occupation, n (%)		
Employed	96 (67.1)	88 (63.3)
Unemployed	19 (13.3)	16 (11.5)
Student	24 (16.8)	29 (20.9)
Other+	4 (2.8)	6 (4.3)
Smoking before pregnancy, n (%)	26 (18.2)	21 (15.1)
Smoking in early pregnancy, n (%)	2 (1.4)	0 (0)
Physical activity [?]3.5 hours a week before pregnancy*, n (%)	115 (80.4)	105 (75.5)
Handgrip strength (kg), mean (SD)	31.5 (5.3)	30.7 (5.3)
Chronic disorders, n (%)**	26 (18)	19 (14)

Table 1

History of depression and anxiety, n (%)		
Depression within the last 10 years	44 (31)	39 (28)
Anxiety within the last 10 years	38 (26)	42 (30)
Comorbid depression and anxiety within the last 10 years	61 (43)	58 (42)
Antidepressants three months prior to conception and/or during pregnancy, n (%)	30 (21)	32 (23)
Psychological well-being, self-reported		
WHO-5, mean (SD)	54.4 (14.8)	56.0 (16.4)

+ Including stay at home mothers

Table 1

	* The weekly amount of physical activity recommended by The Danish Health Authorities recommendations	* The weekly amount of physical activity recommended by The Danish Health Authorities recommendations	* The weekly amount of physical activity recommended by The Danish Health Authorities recommendations	* The weekly amount of physical activity recommended by The Danish Health Authorities recommendations	* The weekly amount of physical activity recommended by The Danish Health Authorities recommendations	* The weekly amount of physical activity recommended by The Danish Health Authorities recommendations	* The weekly amount of physical activity recommended by The Danish Health Authorities recommendations	* The weekly amount of physica activity recommended by The Danish Health Authori ties recomm
	**Chronic disorders: metabolic diseases, respiratory diseases, arthritis, epilepsy and migraine Missing: BMI (2), Educational level (2), Handgrip strength (2) and WHO-5 (2)	**Chronic disorders: metabolic diseases, respiratory diseases, arthritis, epilepsy and migraine Missing: BMI (2), Educational level (2), Handgrip strength (2) and WHO-5 (2)	**Chronic disorders: metabolic diseases, respiratory diseases, arthritis, epilepsy and migraine Missing: BMI (2), Educational level (2), Handgrip strength (2) and WHO-5 (2)	**Chronic disorders: metabolic diseases, respiratory diseases, arthritis, epilepsy and migraine	**Chronic disorders: metabolic diseases, respiratory diseases, arthritis, epilepsy and migraine	**Chronic disorders: metabolic diseases, respiratory diseases, arthritis, epilepsy and migraine	**Chronic disorders: metabolic diseases, respiratory diseases, arthritis, epilepsy and migraine	**Chro disorders: metabo diseases respira- tory diseases arthri- tis, epilepsy and migrain

Table 2

	N	Intervention group	Control group	Mean diff.	95% CI	P value
Primary outcome						
WHO-5 mean 29–34 gw*	270	60.5	58.5	2.0	–1.3 to 5.2	0.2[a]
Secondary outcomes						
WHO-5 mean 8 weeks pp**	183	60.2	54.7	5.5	1.0 to 10.1	0.04[a]
STAI mean 29–34 gw*	270	37.4	37.3	0.04	–1.9 to 2.0	0.9[a]

	N	Intervention group	Control group	Mean diff.	95% CI	P value
STAI mean 8 weeks pp**	182	35.4	36.7	–1.3	–3.8 to 1.2	0.3[a]
GHQ-12 mean 29–34 gw*	270	10.6	11.1	–0.6	–1.7 to 0.6	0.3[a]
GHQ-12 mean 8 weeks pp**	185	10	11.7	–1.7	–3.5 to 0	0.05[a]
EPDS [?]11+, n (%) 29–34 gw*	(¨)	23.0	29.0	(¨)	(¨)	0.32[b]
EPDS [?]11+, n (%) 8 weeks pp**	(¨)	36.0	16.0	(¨)	(¨)	0.15[b]

* Gestational week, ** Postpartum, [a] Constrained linear mixed model, [b] Logistic regression

+ EPDS missing data. 29–34 gw: 22% (intervention group) and 25% (control group), eight weeks pp: 16% (intervention group) and 29% (control group)

Table 3

	N	Intervention group n=133	Control group n=137	95% CI	P value
Preeclampsia, n (%)	269	1 (0.8)	5 (3.6)	0.6–43.4	0.2[a]
Gestational age (days), mean (SD)	269	279.0 (11.5)	280.6 (10.6)	–1.2 to –4.2	0.8[b]
Preterm delivery, n (%)	269	6 (4.5)	5 (3.7)	0.2–2.7	0.7[a]
Induction of labour, n (%)	269	21 (15.8)	37 (27.2)	1.1–3.6	0.02[c]
Mode of delivery, n (%)	269			–0.1 to –0.1	0.7[c]
Spontaneous vaginal delivery		98 (73.7)	98 (72.1)		
Instrumental delivery		12 (9)	17 (12.5)		
Caesarean section		23 (17.3)	21 (15.4)		
Epidural anaesthesia, n (%)	269	46 (34.6)	43 (31.6)	0.5–1.5	0.6[c]
Duration of labour (hours), mean (SD)	247	5.3 (4.0)	5.6 (4.0)	–0.8 to 1.2	0.7[b]
Birth weight (grams), mean (SD)	269	3511 (515)	3501 (500)	–131 to 112	0.9[b]
Birth length (centimeters), mean (SD)	264	52.0 (2.2)	51.7 (2.3)	–0.9 to 0.2	0.2[b]

Table 3					
Apgar score (< 7 at 5 min), n (%)	268	1 (0.8)	1 (0.7)	0.1–16.4	1.0[a]
Arteria pH (< 7.10), n (%)	204	8 (8.4)	10 (9.2)	0.4–2.9	0.9[c]
Exclusive breastfeeding eight weeks postpartum (yes), n (%)	181	66 (67.3)	56 (67.5)	0.6–1.2	0.7[c]
[a] Fischer´s exact test					
[b] Student´s *t*–test					
[c] Chi–square test					

Table 4

	N	**Intervention group n=127**	**Intervention group n=127**	**Control group n=134**	**95% CI**	**P value**
Sick leave yes*, n (%)	244	244	66 (52)	51 (44)	0.20–1.40	0.2[a]
Sick leave days*, median (min–max)	109	109	21.9 (1–150)	20.5 (1–150)	0.56–0.58	0.6[b]
Number of antenatal contacts, median (min–max)	268	268	8.3 (1–24)	8.5 (1–26)	0.91–0.97	0.9[b]
Antenatal telephone consultations, median (min–max)	261	261	2.9 (0–8)	2.5 (0–14)	0.05–0.11	0.1[b]
Length of hospital stay days**, median (min–max)	267	267	3.8 (0–18)	3.7 (0–11)	0.63–0.74	0.8[b]
From baseline until end of intervention	* From baseline until end of intervention	* From baseline until end of intervention				

* Hospitalization in relation to labour
[a] Chi–square test
[b] Mann Whitney *U* test

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